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Original Communications

OBSERVATIONS ON THE PATHOLOGY AND SPREAD OF ENDOMETRIOSIS BASED ON THE THEORY OF BENIGN METASTASIS*

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NORMALLY, endometrium is present only in the uterine cavity, so that any spread of either stroma or glands into other locations is to be regarded as endometriosis. The use of such terms as "adenomyosis," "adenomyoma," "endometrial implants," "endometriosis interna and externa" are descriptive, but the basic pathology is the same, namely, misplaced endometrial tissue. Ordinarily, the heterotopic areas of endometriosis exhibit the same cyclical changes found in the endometrium, even to the development of hyperplasia, adenocarcinoma, decidua, and atrophy, although occasional exceptions have been observed.

Obviously, a functioning endometrium is the precursor of endometriosis. Benign endometrium usually remains quiescent and localized in the uterine cavity up to the menarche, after which it is in a constant normal state of flux, going through the proliferative, secretory, and menstrual phases at regular intervals. This normal growth process has been called *cyclical homeoplasia.*[1] It can lie dormant for many months as in pregnancy, after the completion of which cyclical homeoplasia is resumed.

Benign endometrium may spread (a) by direct invasion of the myometrium (adenomyosis) and of the endosalpinx, (b) by exfoliation of cells through the Fallopian tubes with implantation on the ovaries and peritoneum, (c) by lymphatic metastasis to lymph nodes,[1] (d) by hematogenous metastasis locally[10] and to distant organs such as the kidney.[2, 3] From this, it is readily apparent that the spread follows the same channels taken by endometrial carcinoma.[1, 4] Another striking example of benign invasion occurs in pregnancy when fetal trophoblastic giant cells penetrate the decidua and myometrium and they are even carried to the lungs (deportation) where they are destroyed.

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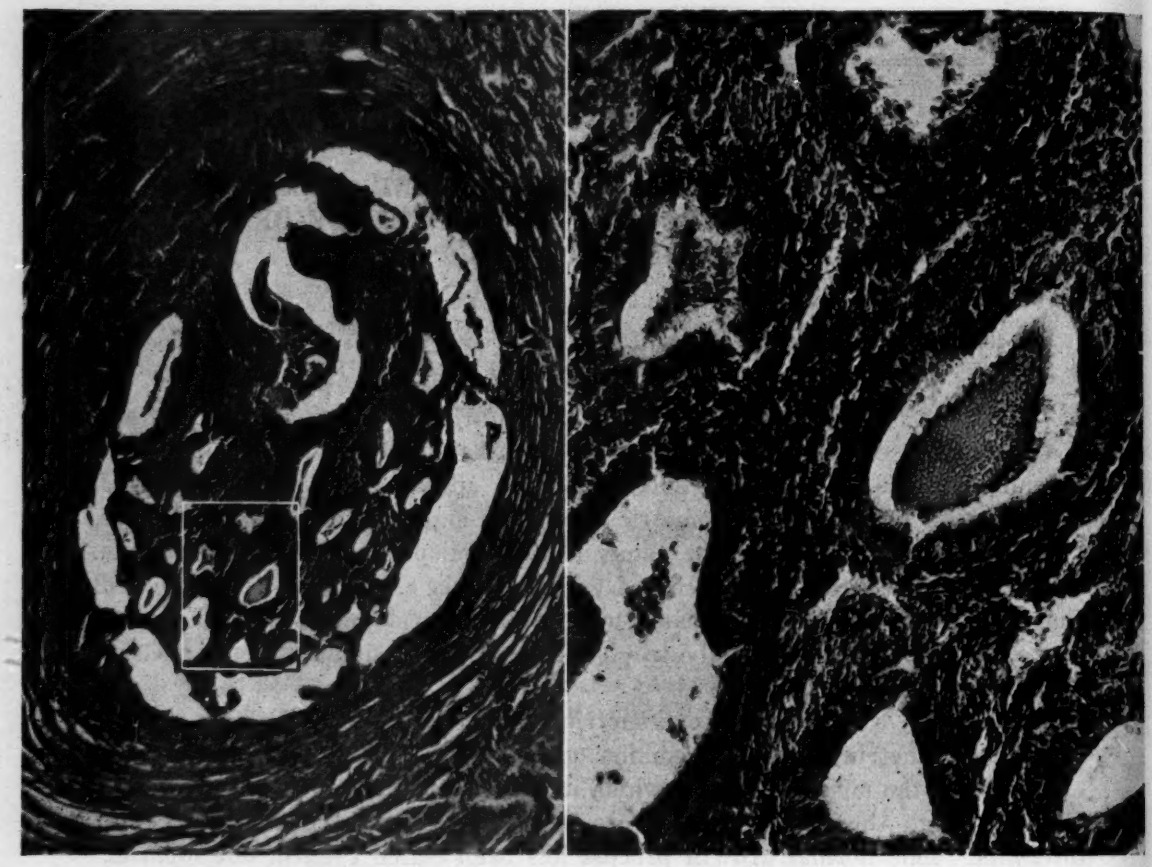
The congenital and celomic metaplasia theories of origin have no place in the author's concept of endometriosis, which is based on the principles of cyclical homeoplasia and benign metastasis.[1] However, an authority who prefers the theory of celomic metaplasia has objected to it.[5] It is difficult to prove or disprove the celomic metaplasia theory of Iwanoff, Meyer and Novak.[1]



A. *B.*

Fig. 1.—*A*, Endometrial tissue invasion of the isthmic portion of the endosalpinx. It can serve as a nidus for exfoliation and subsequent implantation of cells on the serosal surfaces.

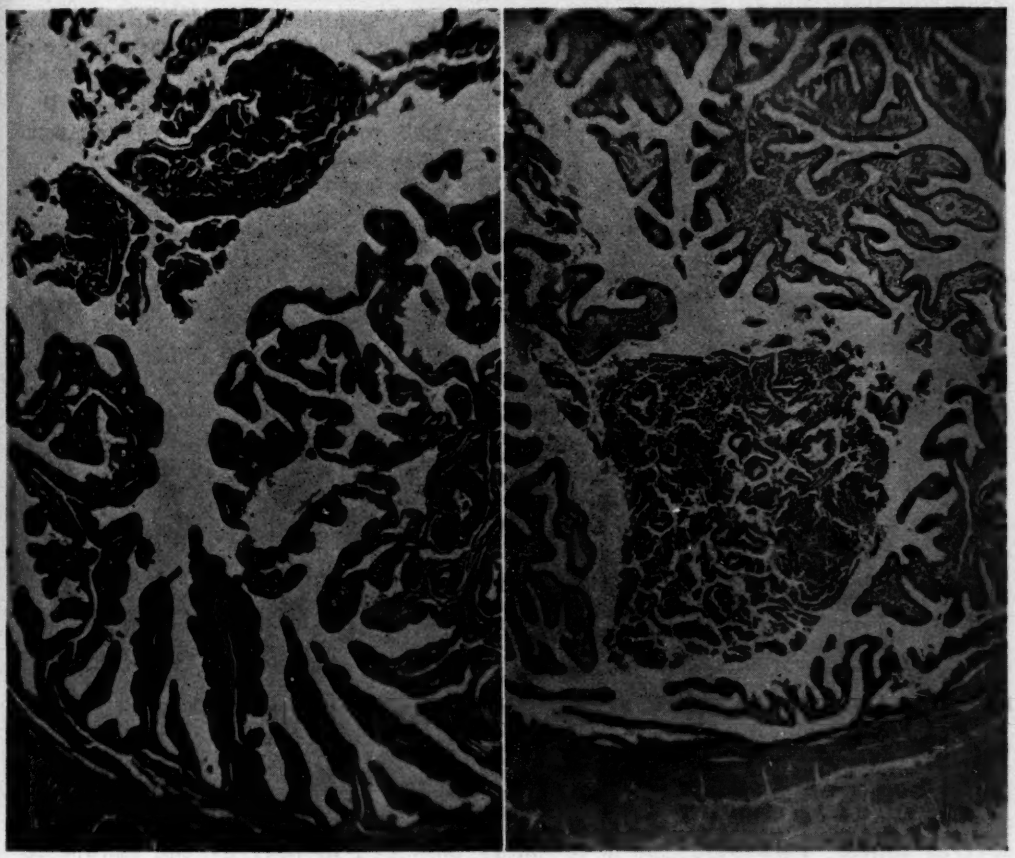
B, Higher power of rectangular area shown in *A*, revealing stroma and glands.

Incidence

All women with functioning endometrium are susceptible to endometriosis. It has not been observed in girls before the menarche, in males, or in those with normal ovaries and rudimentary or absent uteri. Endometriosis has been reported in very young girls after the menarche at ages 12[6]; 13[7] and 15 years.[1] It is essentially a disease of the nullipara or of women with low parity and manifests itself clinically during the childbearing period of life. Constant, repetitious cyclical homeoplasia of the endometrium uninterrupted by pregnancy seems to be the predisposing factor in the development of both endometriosis and endometrial carcinoma. It is of interest that placentation,

adenomyosis, and adenocarcinoma occur most frequently on the posterior wall of the uterine cavity.

The incidence varies a great deal according to the material studied and appears to be highest in the specimens removed from menopausal women. Postclimacteric specimens may reveal atrophic areas of endometriosis having a pattern that is similar to the atrophic endometrium. Contrary to common belief, they do not disappear without a trace after the menopause. Endometriosis is often asymptomatic and is an incidental finding on tissue examination, while some women have distressing clinical symptoms.



A. *B.*

Fig. 2.—*A*, Endometrium found unattached in the midportion of endosalpinx. It has a secretory pattern corresponding with that in the uterus removed on the twenty-sixth day of cycle.

B, The opposite tube from the same patient also contained secretory endometrium.

Material

The diagnosis of endometriosis, including adenomyosis, was made at the time of discharge from the Woman's Clinic in 1,371 patients out of 24,436 patients,[8] which represents an incidence of 5.61 per cent or one in 18 patients over the period from 1933 through 1950 (according to Table I). If patients with adenomyosis are omitted, then there were 599 patients with "external endometriosis," an incidence of 2.4 per cent. A higher incidence was observed on the private service versus the pavilion or ward service, namely 3.6 and 2.0 per cent, respectively.

The diagnosis of endometriosis of the uterus (chiefly adenomyosis) appears in the annual reports[8] from the beginning of the Clinic as indicated in Table I. However, the diagnosis in the ovary was not mentioned until 1936. Endometriosis of the vagina, cervix, and tube were not recorded until 1946 and extragenital endometriosis made its appearance in 1947, while no endometrial lesion has been recorded for the vulva. It is important to point out that the number of admissions increased gradually from 626 in the year 1933 to 2,050 in 1950. During the first decade the incidence remained stationary at 3 to 4 per cent. During the past four years, 763 cases have been observed, or more than half of the total number, giving an incidence of 9.91 per cent. This increase is probably due to a greater interest and awareness of the disease in addition to more opportunities for diagnosis because of more complete hysterectomies and radical pelvic surgery.

TABLE I. THE INCIDENCE OF ENDOMETRIOSIS FROM 1933 TO 1950 IN PATIENTS DISCHARGED FROM THE WOMAN'S CLINIC ACCORDING TO ORGANS INVOLVED

YEAR	TOTAL DISCHARGES	VULVA	VAGINA	CERVIX	UTERUS	TUBE	OVARY	EXTRAGENITAL	TOTAL NUMBER	TOTAL PER CENT
1950	2,050	0	0	1	96	8	54	38	197	9.6
1949	1,923	0	0	3	93	9	70	20	195	10.1
1948	1,966	0	3	2	113	11	95	10	234	11.9
1947	1,755	0	0	0	80	0	66	11	157	8.9
1946	1,722	0	1	1	54	3	12	0	71	4.1
1945	1,489	0	0	0	17	0	0	0	17	1.1
1944	1,423	0	0	0	39	0	14	0	53	3.7
1943	1,268	0	0	0	18	0	33	0	51	4.0
1942	1,367	0	0	0	10	0	32	0	42	3.0
1941	1,339	0	0	0	38	0	21	0	59	4.4
1940	1,248	0	0	0	32	0	12	0	44	3.5
1939	1,282	0	0	0	22	0	22	0	44	3.5
1938	1,289	0	0	0	17	0	23	0	40	3.1
1937	1,173	0	0	0	20	0	24	0	44	3.7
1936	952	0	0	0	33	0	25	0	58	6.0
1935	853	0	0	0	29	0	0	0	29	3.3
1934	711	0	0	0	19	0	0	0	19	2.6
1933	626	0	0	0	17	0	0	0	17	2.7
	24,436	0	4	7	747	31	503	79	1,371	5.61
Incidence endometriosis		0	1:6,000	1:3,500	1:32	1:800	1:48	1:305	1:18	

Obviously, the same patient with endometriosis may have had several admissions during the 17-year period referred to above so as to be counted several times. However, this is probably balanced in part by the failure to recognize the disease in other patients. Be that as it may, the gross statistical incidence of endometriosis based on discharged patients is 1:32 for the uterus; 1:48 for the ovary; 1:305 for extragenital lesions such as appendix, intestine, surgical scars, etc.; 1:800 for the tube; 1:3,500 for the cervix; 1:6,000 in the vagina; while no vulvar involvement has been observed. A considerable number of patients with lesions unconfirmed by histological examination are not included so that these incidences are approximate and based on available data.

Direct Invasion

Benign endometrial stroma and glands can spread along the lymph and blood channels of the myometrium[9, 10] as well as between the individual muscle fibers, producing the well-known lesion of endometriosis known as "adenomyosis uteri." Not infrequently, the endometrium may be found attached to the endosalpinx of the tube.[11] We regard this as invasion of the endosalpinx

and have observed it in sections of the isthmic portion in 6 out of 30 patients, one of which is shown in Fig. 1. Similar lesions have been observed in the middle of the tubes in other cases. Exfoliation of endometrial cells from such a nidus in the endosalpinx may produce implants on the pelvic organs.[1]

Implantation

Regurgitation at menstruation of endometrial cells through the Fallopian tubes may provide for the surface implants of endometrium on the serosa and peritoneum.[12, 13, 19] This concept has been proved experimentally in the monkey.[15] Unattached endometrium in the secretory phase of the cycle has been observed in the midportions of both tubal lumina removed by panhysterectomy on the twenty-sixth day of the menstrual cycle. They are shown in Fig. 2. The specimen including the tubes was fixed in formalin before sectioning which minimizes the possibility of "artefact." The regurgitated endometrium resembled that in the uterus. At laparotomy following curettage in another patient, a blood clot was found at the fimbriated end of one tube and it contained endometrial tissue shown in Fig. 3. The "powder burn" scars on the serosal surface of the uterus, tubes, uterine ligaments, ovaries, pelvic peritoneum, intestines, appendix are examples of implantation.

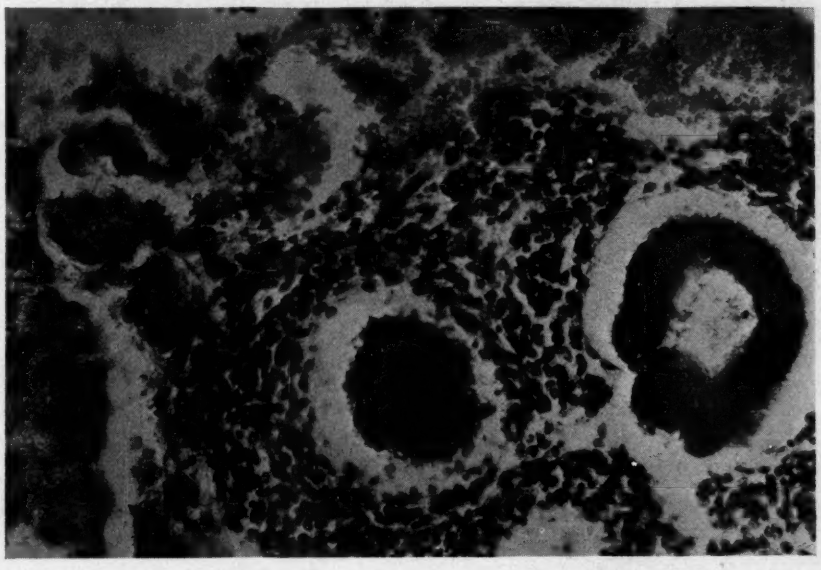


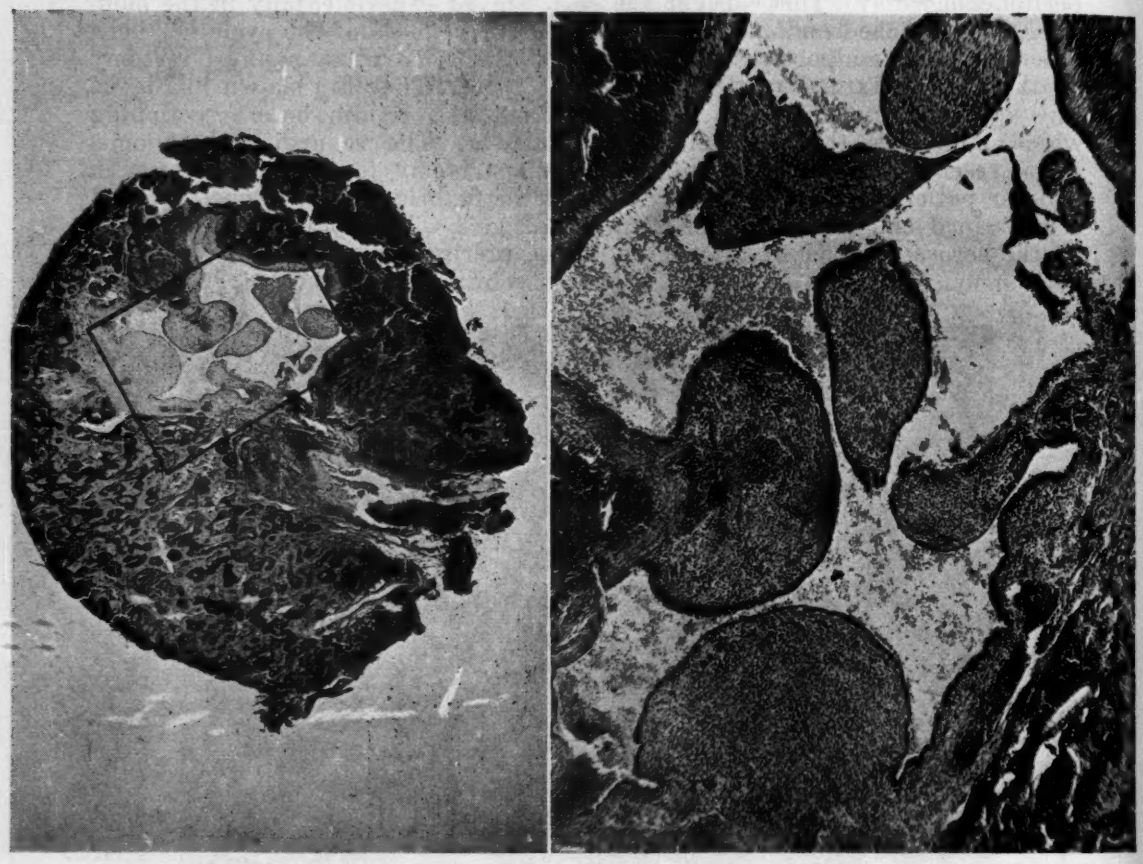
Fig. 3.—Endometrium found in blood clot removed from fimbriated end of the tube. Laparotomy was performed immediately after dilatation and curettage. The glands have a proliferative pattern.

Transplantation of endometrial tissue has been seen in many laparotomy scars and in an episiotomy scar.[15] We have seen such a lesion in the abdominal scar following therapeutic abortion and tubal sterilization. Exfoliated cells from a nidus of endometriosis in the endosalpinx as in Fig. 1 may also implant themselves.[1] Finally, secondary 'implants" may develop by spread of cells from other foci previously established.

Lymphatic Metastasis

Endometriosis has been reported in the inguinal lymph nodes[17, 18, 19] and also in the pelvic lymph nodes.[1, 20] The lesion shown in Fig. 4 represents a ureteral node with endometrium and indicates spread by the lymphatic channels. Lymphatic or venous spread probably accounts for some of the extra-

peritoneal lesions of endometriosis found in the cervix, vagina, vulva, broad ligament, as in Fig. 5, muscularis of the tube, hilum of ovary, bladder, ureter, intestine, groin, and perhaps the umbilicus. The large lesion in Fig. 6 was found in the subcutaneous fat of the abdomen, without history of previous laparotomy, located above the fascia well below and to the left of the umbilicus, with no hernial communication with the peritoneal cavity. It is probably the result of either lymphatic or blood-stream metastasis.



A. *B.*

Fig. 4.—*A*, Endometrial tissue in hilum of the left hypogastric lypmh node. *B*, Higher power of area designated in *A*.

Hematogenous Metastasis

Hematogenous spread was suggested by Sampson[10] when he found endometrial tissue growing in the venous blood vessels of a uterus containing adenomyosis. We have confirmed this observation in five uteri with adenomyosis, having never observed it in a normal uterus. Endometrial tissue is shown in venous channels of the uterus in Figs. 7 and 8 and also in a venous vessel of the tube as in Figs. 5 and 9. Elastic tissue stains were confirmatory. Actual stromatosis vascularum of the uterus has been observed about 15 times in the five uteri, two of which are shown in Fig. 8. The degree of lymphatic and hematogenous spread is probably extreme in those patients with "frozen pelvis."

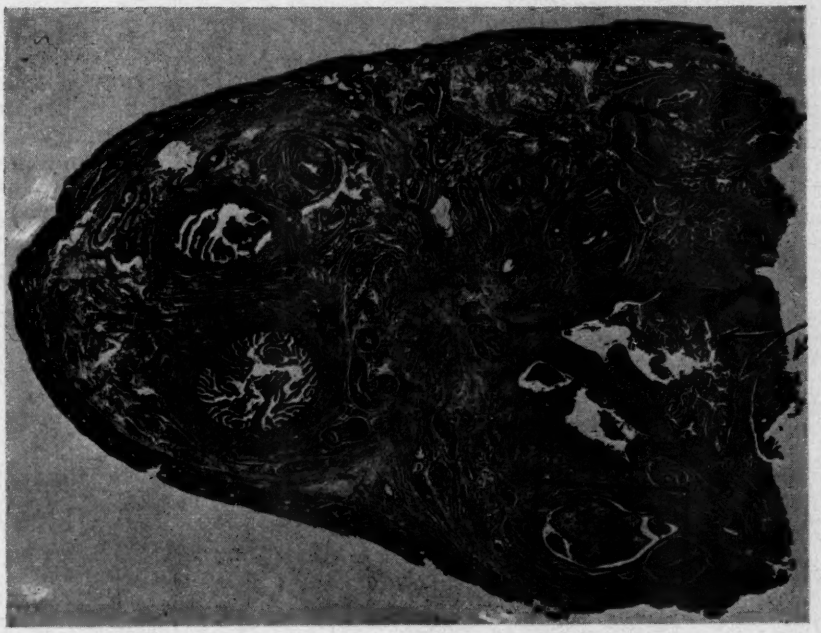
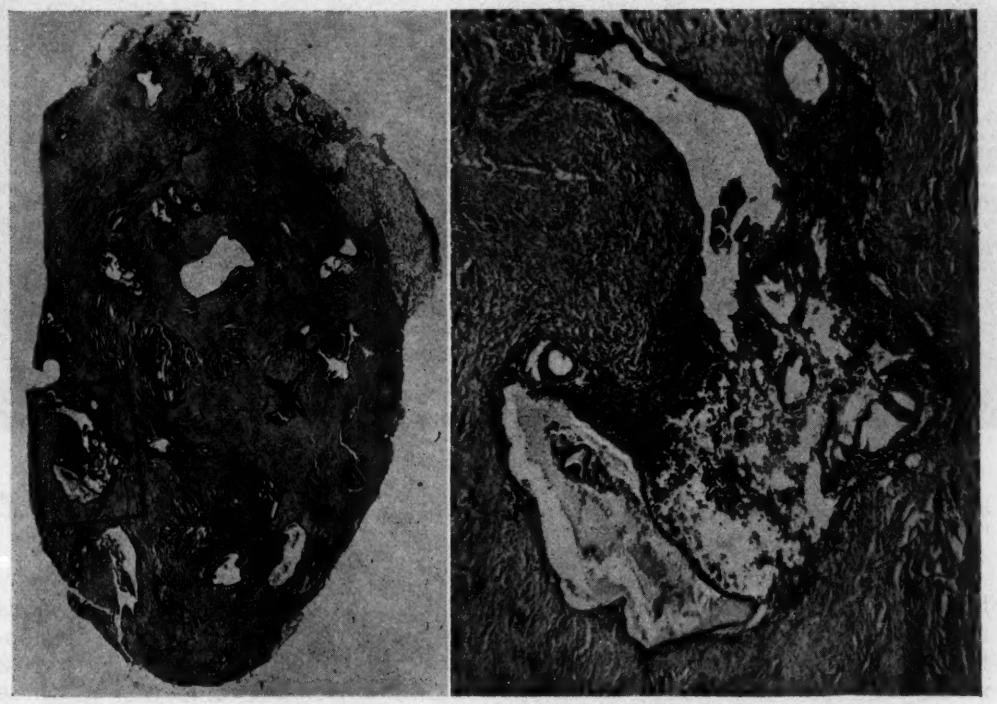


Fig. 5.—Macrophotograph of broad ligament to show endometrial lesion (at arrow) without connection to peritoneum suggesting lymphatic spread. Blood vessel in rectangle is shown in Fig. 9.

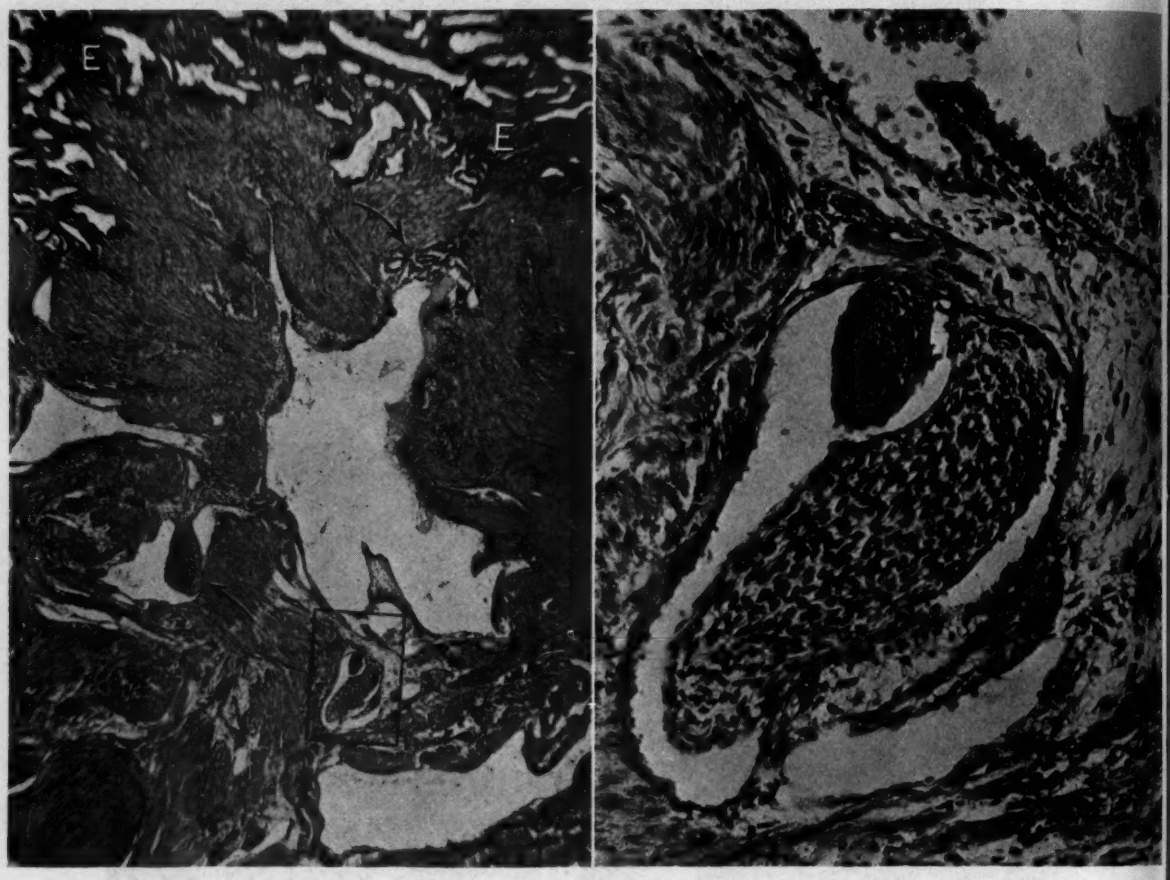


A. *B.*

Fig. 6.—*A*, Subcutaneous endometriosis of the lower anterior abdominal wall without previous laparotomy.

B, Higher power of rectangular area shown in *A*.

Evidence is slowly accumulating in the literature suggesting spread via the blood stream beyond the uterus and tubes. Consideration must be given to such metastasis to explain the distant lesions in the forearm, thigh, axilla, hand, and kidney.[1] Marshall's observations on the kidney[2] have been recently confirmed by Maslow and Learner.[3] The occurrence of pulmonary and brain lesions would give this view great impetus. However, lung endometriomas appear to be exceedingly rare, most likely because of the infrequency of lobectomies in young women, so that pathologists simply have not had the opportunity for adequate observations. There is only one recorded case of benign adenomyomas of the lung.[21] However it has been shown experimentally[22] that

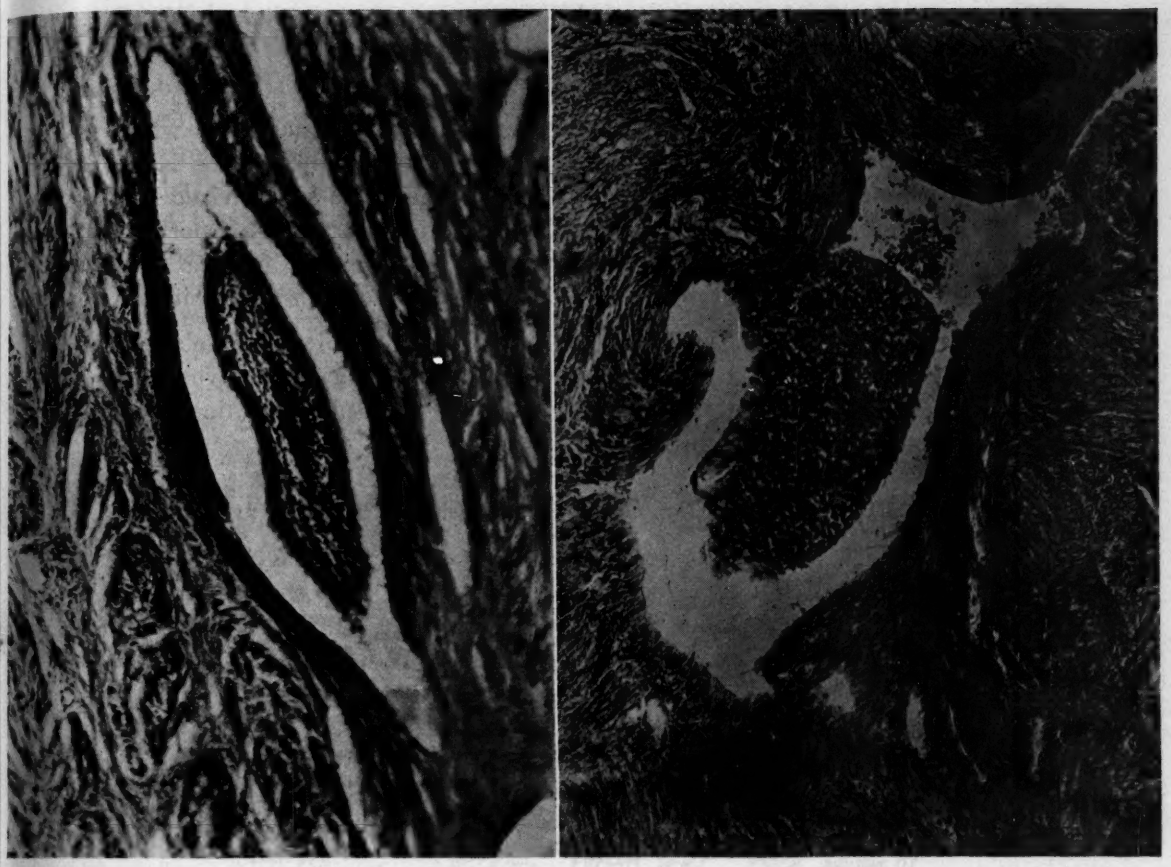


A. *B.*

Fig. 7.—*A*, Low-power view of endometrial stroma present in a large venous blood sinus of the myometrium just below the basal layer of the endometrium at *E*. Similar areas indicated by arrows.

B, Higher power of area designated in *A*.

hematogenous dissemination of endometrium can produce pulmonary lesions in rabbits. A young woman with x-ray evidence of a lung tumor with hemoptysis was cured by castration.[23] Perhaps preliminary fixation and gross serial section of the lungs at autopsy would aid in the detection of these lesions. On the other hand, trophoblastic cells disappear without a trace in the lung after pregnancy and perhaps the benign endometrial cells are similarly destroyed. Pulmonary metastases of endometrial cancer cells have been observed in only seven per cent of patients.[1] Evidently the lungs can also destroy the malignant emboli.[24]



A. *B.*

Fig. 8.—Stromatosis vascularum of uterus. *A*, Endometrial stroma without glands in a venous blood vessel of the myometrium of a patient with adenomyosis uteri. *B*, Similar lesion of another case. Note red blood cells in lumen.

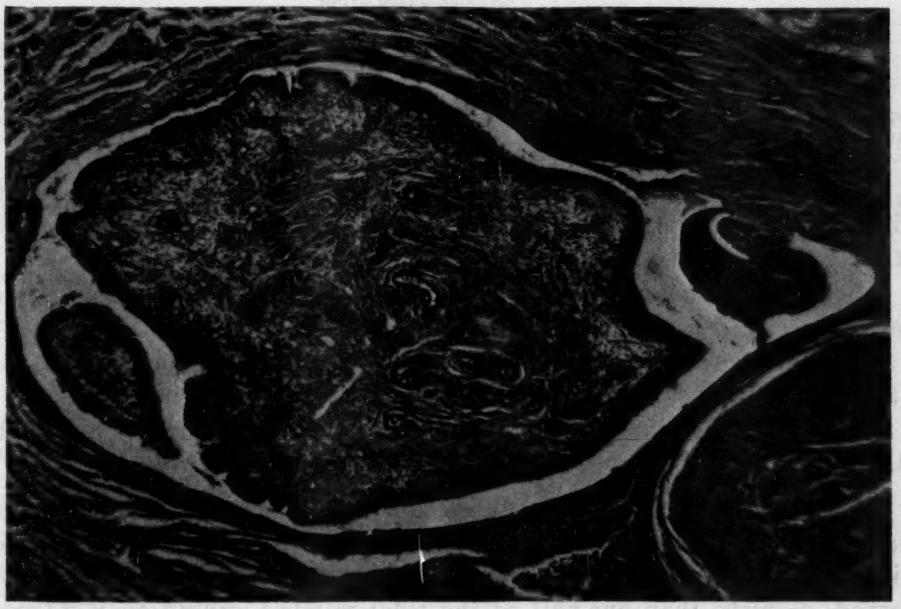


Fig. 9.—Endometriosis vascularum of tube. Endometrial stroma and glands in a venous blood vessel. This is high power of rectangular area in Fig. 5.

Summary

Normally, benign endometrium is confined to the uterine cavity where it undergoes cyclical homeoplasia. The spread of benign endometrium is essentially the same as for endometrial carcinoma and has been summarized in Fig. 10. It governs the location of the various genital, extragenital, peritoneal, and extraperitoneal lesions of endometriosis. In addition to cyclical homeoplasia, the composite theory of benign metastasis for endometriosis includes:

1. Direct extension either into the lymphatics or blood vessels of the myometrium or between the muscle bundles, producing adenomyosis uteri. Direct extension may also take place into the endosalpinx forming a nidus of endometrium for the exfoliation of cells.

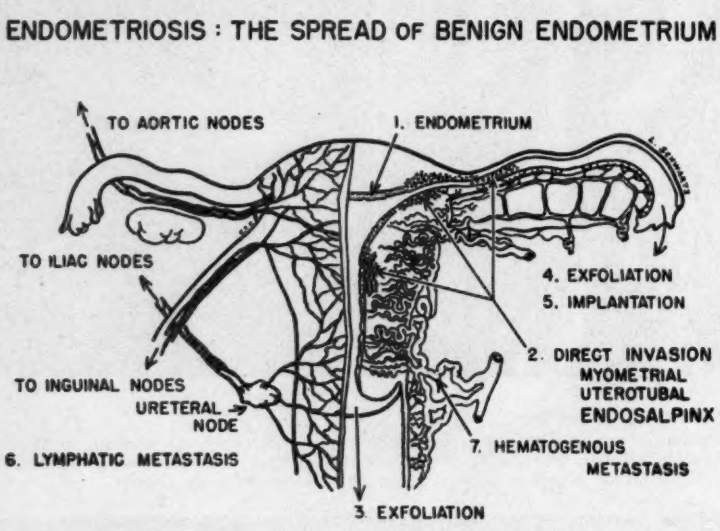


Fig. 10.—Diagram showing spread of benign endometrium along proved channels on which the theory of benign metastasis is based. (Modification of similar diagram published by author in Cancer 2: 399, 1949.)

2. Exfoliation and implantation of endometrial cells at menstruation, during curettage, or from a nidus in tube to produce lesions on peritoneal surfaces.

3. Lymphatic spread with involvement of lymph nodes and adjacent organs.

4. Venous spread in uterus and tubes and hematogenous metastasis to distant organs such as the kidney.

5. Secondary lesions from foci already established along the above channels.

The composite theory of benign metastasis for the spread of endometriosis is based on an experience with 1,371 patients during the past 17 years, or a clinic incidence of 5.61 per cent. During the past four years, 763 patients were observed, or more than one-half of the total number, giving an incidence of

9.91 per cent. This apparent increase coincides with the tendency toward smaller families, widespread use of contraception, fewer cervical dilatation and fewer uterine suspension operations, and more intravaginal tampons during menstruation.

Not every patient with endometriosis will exhibit the entire pattern of dissemination since there are other related factors including: age at onset, hormone balance, cervical stenosis, retroversion, intravaginal tampons, sterility, parity, tissue resistance and reaction, duration of the disease, type of pelvic surgery (conservative, castration), radiation, testosterone, and pregnancy. Young patients may require a dilatation and curettage, excision of pelvic lesions and adhesions, conservation of ovarian function, and uterine suspension, after which they are urged to conceive at once. Pregnancy is the best prophylactic and curative treatment for endometriosis, since it interrupts the cyclical homeoplasia during which time the endometrium lies dormant. Each pregnancy reduces the period of growth for the endometrium by approximately 12 months.

The incidence of further spread or recurrence after conservative surgery depends on the original extent of the process, the success of the operation, and the number of pregnancies. In older women, total hysterectomy and bilateral salpingo-oophorectomy may become the procedure of choice, rather than castration by irradiation since the latter may stimulate the endometrium to develop adenocarcinoma, as has been observed in several patients. Furthermore, it has been shown[1] that endometrial carcinoma occurs with greater frequency in patients with endometriosis.

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CERTAIN CONCEPTS IN THE HANDLING OF BREECH AND TRANSVERSE PRESENTATIONS IN LATE PREGNANCY*

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ONLY recently the author has made certain observations[1, 2] concerning the effect of the position of the in situ placenta, in women late in pregnancy, upon the axis polarity of the amniotic sac and upon the presentation of the fetus it contains. These have led to a realization of the etiology of breech and transverse presentations of the fetus in single pregnancies in the last weeks of gestation. This information requires a reorientation in our thinking concerning the use of external version for the correction of fetal malpresentation.

In 1807 Wigand[3] wrote of his discovery that the position of the fetus could easily be altered by manipulations through the abdominal wall, and Hubert,[4] in 1843, wrote of his experiences in the correction of "vicious" presentations of the fetus by external manipulations. The section on external version in Pinard's[5] classic *Treatise on Abdominal Palpation,* which appeared in 1889, gave great impetus to the utilization of external version, and the use of this maneuver has since enjoyed periodic surges of popularity, and some small continuous usage here and there in the obstetric world.

Twenty years ago the representative thought at that time regarding the handling of breech and tranverse presentations in the latter part of pregnancy was well stated by the late J. Whitridge Williams[6] when he wrote, "If a breech or transverse presentation is diagnosed in the last weeks of pregnancy, its conversion into a vertex should be attempted by external maneuvers, provided there is no marked disproportion between the size of the child and the pelvis. Cephalic version is indicated by reason of the increased foetal mortality attending spontaneous delivery in breech presentation; while if the child lies transversely a change of presentation is imperatively demanded, inasmuch as a natural labor is out of the question, and if appropriate measures are not adopted the lives of both mother and child will be lost." This certainly must be construed as a hearty endorsement of external version by one of the great modern obstetricians. One wonders to what extent this holds true today, because external version of fetuses presenting by the breech does not now appear to be a commonly employed practice.

Williams[7] employed this maneuver in "hundreds of patients" and did not find that it gave rise to twisting of the cord or to the coiling of loops of cord about the fetus, nor did he have occasion to believe that it caused damage to, or premature separation of, the placenta. The similar experience of many obstetricians is reflected in the publications of Irving,[8] Glassman,[9] Danforth and Galloway,[10] Gibberd,[11] Newell,[12] Gordon,[13] Goethals,[14] Siegel,[15] Ryder,[16] Mc-

*Presented, by invitation, before the Columbus, Ohio, Society of Obstetricians and Gynecologists, Nov. 30, 1950.

Guiness,[17] Donovan,[18] and Thornhill,[19] to mention a few. These authors have generally believed that external cephalic version is a safe and easy maneuver for mother and fetus in most single pregnancies. They also believed that the risk to the mother and baby from external cephalic version followed by vaginal delivery of a cephalically presenting fetus was several times less than that attendant upon breech delivery.

Material

We have recently determined,[1] in a series of 52 cases of transverse or oblique presentation of the fetus, that the placenta was implanted in the general fundal region of the uterus in 46 per cent of the cases (Table I), and in the lower uterine segment in 44 per cent. Included in this lower uterine segment group is an incidence of placenta previa of 27 per cent for the entire series. These figures are far in excess of normal averages. The normal average figure for the occurrence of implantation of the placenta in the fundus (Table I) was only 9.9 per cent in a large series of cases, and we have long known that placenta previa has an incidence of only about 0.6 per cent. Compared with these normal occurrence rates, the incidence of fundal implantation in our series of 52 cases of transverse presentation was fivefold in excess, and the incidence of placenta previa 70 times in excess. This correlation leads us to conclude that the major cause of transverse or oblique presentation of the fetus in the last ten weeks of pregnancy is the implantation of the placenta in the fundus of the uterus or in the lower uterine segment. Such placental implantation (Fig. 1) tends to make the amniotic sac more spherical and less ovoid in shape than is the case when the placenta is implanted on the anterior or posterior wall of the uterus. Thus the ovoid fetus curls up as best it can (Fig. 2) in a somewhat spherical space, there being no particular polarity of its containing amniotic sac to invite permanent orientation of the fetus. We find a greater than average fetal motility in cases of this type during the last six to eight weeks of pregnancy, but the position of the fetus varies chiefly between transverse and oblique presentation. The factor of multiparity, with its relatively greater relaxation of the uterus and anterior abdominal wall (which tend toward a more spherical uterus), acting in conjunction with the implantation of the placenta in the fundus or the lower uterine segment, also favors transverse or oblique presentation of the fetus. This point is demonstrated by the fact that the average parity of the women in our transverse presentation series was 3.62, while that of all the patients delivered in this same hospital during the period from which the series was drawn was only 2.38.

It also has been determined, in cases of single pregnancy with breech presentation persisting until term,[2] that the characteristic placental implantation site (Fig. 3) is in the cornual-fundal region of the uterus, on one side or the other, and that the placenta may be directly lateral, partly in the anterior fundus, or partly in the posterior fundus (Fig. 4). Soft-tissue placentography x-rays taken on a series of 76 women with breech presentation in single, term pregnancies[2] (Table I) revealed that in every case the placenta was implanted in one cornual-fundal region of the uterus or the other.

In seeking substantiation for our findings in historical records, we have found the placenta to be implanted in the left cornual-fundal region of the uterus in an artist's conception of a "frozen section" of a woman with breech presentation who died undelivered at term, as credited to Waldeyer.[20] We found the same situation existing in a similar case ascribed to Williams.[21] Titus[22] also pictures a "frozen section" of a uterus in which the fetus is presenting by the breech; its head lies in the left cornu, and the placenta is implanted in the right cornual-fundal region. This characteristic position of the

TABLE I. A COMPARISON OF THE GENERAL PLACENTAL IMPLANTATION SITES, EXPRESSED IN PERCENTAGE OF OCCURRENCE, IN THE NEAR-TERM UTERUS IN A SERIES OF CASES OF BREECH PRESENTATION, A SERIES WITH PERSISTENT TRANSVERSE OR OBLIQUE PRESENTATION, AND A SERIES IN WHICH THE INCIDENCES OF THE VARIOUS FETAL PRESENTATIONS WERE OF RELATIVELY NORMAL OCCURRENCE

FETAL PRESENTATION	MID-FUNDUS	ANTERIOR FUNDUS	POSTERIOR FUNDUS	RIGHT FUNDAL-CORNUAL REGION	LEFT FUNDAL-CORNUAL REGION	MID-ANTERIOR WALL	MID-POSTERIOR WALL	MID-LATERAL WALL	LOW ANTERIOR WALL	LOW POSTERIOR WALL	PLACENTA PREVIA
All fetal presentations of normal average occurrence (681 cases)	7.1	1.9	0.9	"Tubenecken Placentae" 7.3		35.7	34.3	9.4	1.0	1.8	0.6
Breech presentation (76 cases)	0	0	0	29	71	0	0	0	0	0	0
Transverse or oblique presentation (52 cases)	25.0	15.4	5.8	0	2.0	7.6	0	0	11.6	5.8	26.8

Note above that the average occurrence of implantation of the placenta in the fundus of the uterus, regardless of fetal presentation, is 9.9 per cent, whereas in cases of transverse of oblique presentation the incidence is 46.2 per cent, and that only 3.4 per cent of placentas, generally, are implanted in the lower pole of the uterus, while in 44.2 per cent of the cases with transverse presentation the placenta was so implanted. The direct relationship betwen placental implantation in either pole of the uterus and transverse presentation of the fetus is obvious, and these particular placental sites have been shown to be the chief cause of this presentation.[1]

In the series of 76 cases of breech presentation the placenta was implanted only in one cornual region or the other, and such placental implantation site has been shown to be the principal cause of breech presentation in single pregnancies in the last weeks of gestation.[2]

placenta in breech presentation, thus, has been demonstrable for years. We believe that the principal cause of persistent breech presentation in single term, or near-term, pregnancies is the cornual-fundal implantation of the placenta, since it occurs (Table I) in only 7.3 per cent of all pregnancies and yet was present in every case in our series[2] of 76 women with breech presentation.

The anatomic relationships between the uterus, placenta, and amniotic sac are such, as demonstrated in Fig. 3, that the axis polarity of the sac, as a result of the placental implantation in the cornual-fundal region of the uterus, is changed from the polarity of the uterus. The smaller pole of the amniotic sac ovoid now lies in the cornu opposite to that which contains the placenta, and the larger pole of the sac lies chiefly in the lower uterine segment. The fetus, in obeying the Law of Accommodation, fits itself into the shape of the amniotic sac so that its head (its smaller pole) lies in the smaller pole of the sac, while its breech and legs (its larger pole) rest in the sac's larger pole. The cornual-fundal placenta, causing, as it does, a near-reversal of the polarity of the amniotis sac from that of the uterus, is such *a potently active cause* of breech presentation that about one-fourth of fetuses successfully turned from breech to cephalic presentation by external version spontaneously revert to breech.[12] From this it would seem that the fetus strives, in a positive manner, to accommodate itself properly to the shape of the amniotic sac.

These findings, with regard to the placental implantation sites characteristic of breech and transverse presentation in the last weeks of pregnancy, have led us to propose a new obstetrical principle: *In term or near-term human pregnancies, when the placenta is implanted chiefly in the fundus, the lower uterine segment, or in either cornual region of the uterus, as it indents and alters the ovoid shape of the amniotic sac, it obliterates the polarity of the sac or determines it independently of the fixed polarity of the containing uterus; functionally, the fetus accommodates itself to the shape of the sac, the fetal head seeking its smaller pole; and thus the placental implantation site has a determining effect upon the presentation of the fetus.*

We believe that our findings regarding fetal presentation prove the old Theory of Accommodation and detract from the validity of the theory of the effect of gravity upon fetal presentation; we believe that the fetal head will seek the smaller pole of the amniotic sac (if there is such a pole) regardless of where this pole happens to be located in the uterine cavity.

A knowledge of the typical placental positions in the uterus in patients with breech and transverse presentations of the fetus can be of considerable value when correctional external cephalic version of the fetus is being contemplated.

External Cephalic Version

External version is practiced in many of the leading clinics of this country and, in the hands of most experienced obstetricians, it carries no discernible risk to the fetus or mother. When it can be performed successfully it obviates the fetal mortality of breech delivery of from 2.7 per cent, as reported by Tompkins,[23] to 10 per cent, as stated by Beck.[24] Tompkins' figure is corrected to exclude all premature and abnormal infants, twins, and those who died of conditions not connected with breech delivery per se, whereas Beck's figure includes all cases. The figures from five maternity services, reported by Dieckmann,[25] give a gross fetal mortality for breech delivery of 7.7 per cent, which is similarly corrected to 4.2 per cent.

Despite the improvement of the fetal survival rate in breech delivery in the past two decades it still would appear that the performance of external

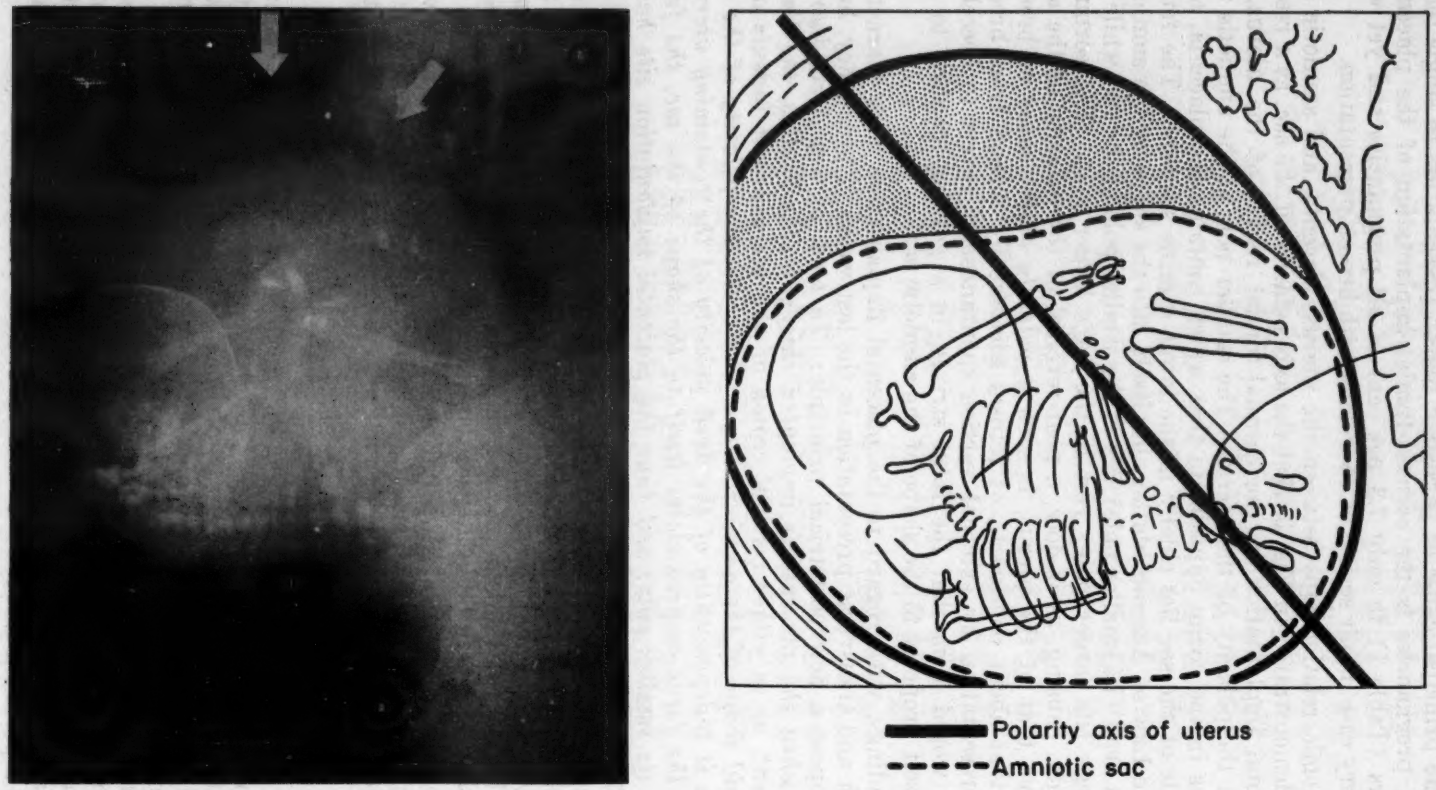

Fig. 1.—Mid-fundal implantation of the placenta.

Left lateral soft-tissue x-ray of a near-term pregnant uterus with accompanying diagrammatic sketch made from a direct transparency tracing of the film. The implantation of the placenta in the fundus of the uterus has caused the amniotic sac to assume a more or less spherical shape and to be without any specific polarity. In accommodating itself to the shape of the sac the fetus has therefore assumed a transverse lie. A polarity axis can be drawn through the contour of the uterus, but such polarity cannot be demonstrated in the amniotic sac. (Arrows delineate the fundus.)

cephalic version of fetuses presenting by the breech is good obstetric practice. If the day arrives when breech delivery is conducted generally throughout the country with such skill that the fetal mortality figures, both corrected and uncorrected, closely approach those for cephalic delivery, then there will no longer be a need for the maneuver, external cephalic version. Or, if reliable figures for fetal and maternal mortality arising from the mere performance of external version could ever be computed and it is found that they closely approach the fetal and maternal mortality rates for breech delivery, then external version can be cast aside.

What is the danger to the fetus and mother when external version, for conversion of breech to cephalic presentation, is performed? Ryder,[16] who reported having done external version personally in 290 cases in a series of 1,700 private patients, stated that not one fetus could be shown to have suffered any harm. In his series there was no vaginal bleeding nor any maternal mortality in cases in which external version was performed. He did, however, have fetal death in one case with placenta previa, which, he stated, was not the result of external version, and in another from "accidental hemorrhage." This brings up the important points that *external version should not be performed upon patients who have placenta previa,* and that the version in the case with subsequent vaginal bleeding might have caused some placental separation, although this possibility is remote since the bleeding occurred eight weeks following the version. Trubkowitch[26] reported on 293 cases of successful external version in patients with breech and transverse presentation, and stated that in these cases the fetal mortality was the same as that in 96,948 women with cephalic presentation delivered during the same period.

Adair[27] collected statistics on 1,105 attempted external versions done by nine authors and found that vaginal bleeding occurred in only two instances, presumably from slight placental separation. A case was reported by Casalta[28] in which abruption of the placenta, with profuse hemorrhage, occurred six hours following external version. The patient delivered a stillborn infant. Examination of the placenta disclosed the presence of two large fresh blood clots in slight depressions in the placenta, and there was no doubt in that author's mind but that the external version he had performed caused the placental separation. Goldenberg reported two such cases, both of which resulted in stillborn infants; one of these mothers also died and a Couvelaire uterus was demonstrated at autopsy, which uterine condition, if truly such, would seem to indicate that she had toxic abruption of the placenta rather than traumatic abruption.

Newell[12] reported on 793 patients at the Boston Lying-in Hospital in whom breech presentation was detected in the third trimester of pregnancy. In all, 1,161 external cephalic versions were attempted, or 1.46 versions per case. Successful turning of the fetus was accomplished in 829 cases, or 72 per cent; spontaneous recurrence of breech presentation following successful external version occurred in 27 per cent of the cases, and was again corrected each time. At term only 20.8 per cent of the primiparas in the series and 6.4 per cent of the multiparas still had breech presentation. Spontaneous cephalic version occurred 108 times, or in 19.3 per cent of the cases, and this event took place either in those patients in whom the attempt at external version had been unsuccessful, or in some of those in whom the fetus had reverted to breech presentation following successful external version. The net result in this series, at the onset of labor or at the time of delivery, was that only 10 per cent of the patients still had fetuses presenting by the breech, while those in three women presented transversely. All the rest had cephalic presentation. There was no

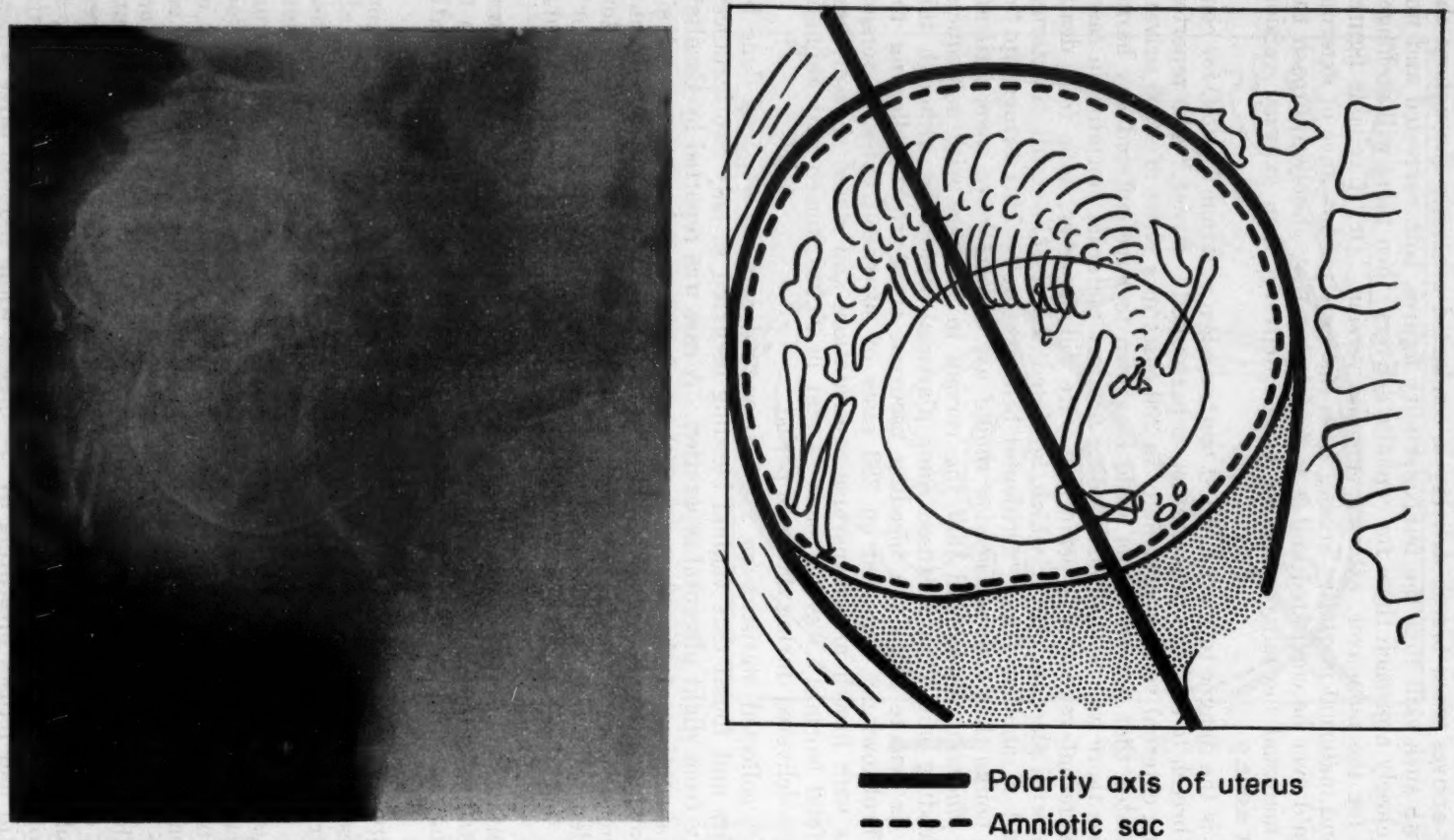

Fig. 2.—Central placenta previa.

Left lateral soft-tissue x-ray of a near-term pregnant uterus with accompanying diagrammatic sketch made from direct transparency tracing of the film. Here again the implantation of the placenta in the lower pole of the uterus has resulted in a spherical shape of the amniotic sac with loss of any specific polarity axis. The fetus, in accommodating itself to the shape of the sac, naturally lies in transverse presentation. One can readily draw a polarity axis through the uterus, but no specific polarity of the amniotic sac can be demonstrated.

maternal mortality. The gross fetal mortality was 4.03 per cent, while the corrected figure was 2.9 per cent. In six cases, in which external version had been unsuccessful, neonatal death followed breech delivery. Only seven patients in the entire series had slight vaginal spotty bleeding, which occurred from one to six weeks following version, and all seven infants were born alive. The diagnosis of separation of the placenta was made in four cases, and in three patients it occurred from seven to nine weeks following version, and these three infants were born alive. In the fourth case version was mistakenly attempted on twins, and one week later some placental separation occurred, the patient went into labor, and delivered living twins at 36 weeks, but they shortly died. When the corrected fetal mortality in this series, 2.9 per cent, is compared with the figure of 4.2 per cent for breech delivery, which is derived from the pooled cases of five maternity hospitals,[25] one cannot fail to be impressed by the value of external cephalic version in breech presentation. Indeed, it can be calculated that the employment of this maneuver saved the lives of 10 or 11 infants in the series reported by Newell.[12] This constitutes a decrease in the usual figure for fetal mortality in breech delivery, in those cases successfully turned, of about 30 per cent, which is a betterment of fetal survival statistics any obstetrician would readily wish to achieve.

The data cited in the foregoing reports certainly reveal the definite possibility of placental damage and separation in any instance in which more than the lightest manual force is exerted in performing external version. They also reveal the fact that when external version is properly performed it can be an extremely valuable procedure. And it can be a relatively safe procedure, provided that the membranes are intact and at least an appreciable amount of amniotic fluid is present and that polyhydramnios is not present, provided that the breech is not firmly engaged and too low in the pelvis to be safely dislodged, that a bicornate uterus is not being dealt with, that placenta previa is not present, and that the abdominal wall is not too obese to permit the necessary manipulations. Except in very experienced hands external version is generally conceded to be inadvisable if anesthesia is necessary to insure relaxation and the cooperation of the patient. External version is contraindicated in cases of multiple pregnancy, where there is any history of vaginal bleeding or of previous extensive myomectomy or previous section, in women who have marked pelvic contracture, and when there are marked deformities of the fetus such as hydrocephalus or anencephalus.

Since we now know that the placenta is implanted in one cornual-fundal region or the other in practically all cases of single pregnancy with breech presentation persisting after 34 weeks of gestation, it is essential to determine in which position the placenta lies (Fig. 4) before doing the version. This can be accurately determined by soft-tissue placentography x-rays, or, in the absence of x-ray facilities, a fairly accurate general idea of which cornu of the uterus the placenta occupies can be gained by palpating the fundus and determining on which side of the midline the fetal head lies. If, for example, the head lies slightly or wholly to the right, then one can deduce that the placenta is implanted in the left cornual-fundal region, and it can easily be avoided in the maneuvering of the fetal poles.

The following are some important general concepts one should bear in mind when performing external cephalic version: The fetal head usually should be pushed in the direction it is facing since this will increase the general flexion of the fetus (Fig. 3); the more the fetal spine can be flexed, with the fetus thus converted more nearly into a sphere, the more easily the fetus can be turned in the uterus. Conversely, if the fetus is in an extended attitude (Fig. 5) it comprises an elongated ovoid and will be very difficult or impossible to turn

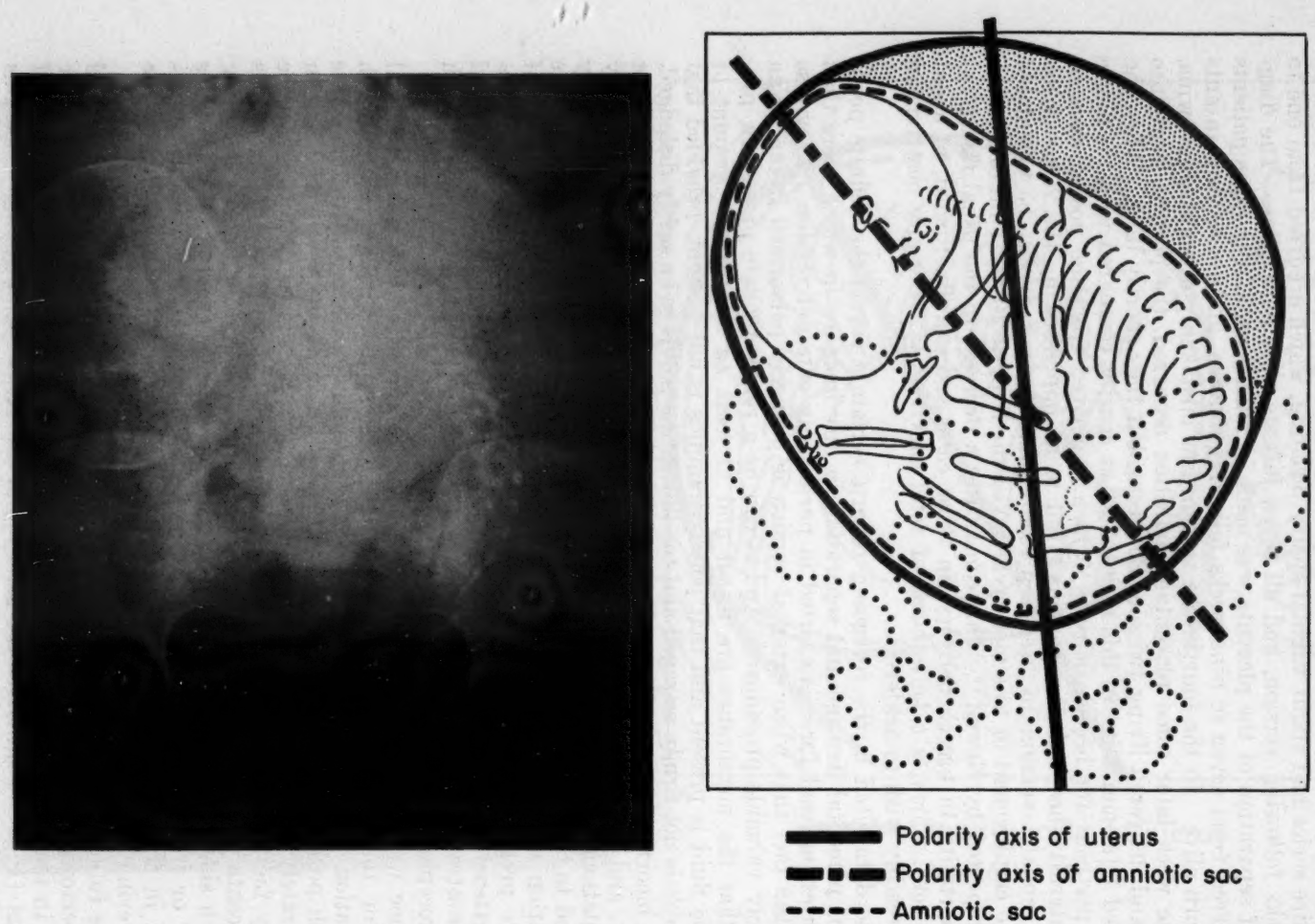

Fig. 3.—Left cornual-fundal implantation of the placenta.

Anteroposterior soft-tissue x-ray of a near-term pregnant uterus with accompanying diagrammatic sketch. The placenta is seen to be implanted in the left cornual-fundal region of the uterus, and this has caused the shape of the amniotic sac to be considerably changed from that of the containing uterus. The sac has a polarity different from and entirely independent of that of the uterus, the smaller pole of the amniotic sac ovoid now lying in the right cornu of the uterus, while its larger pole principally occupies the lower uterine segment. The fetus, in accommodating itself to the shape and polarity of the amniotic sac, lies with its head in the smaller pole of the sac ovoid and its breech and legs (which comprise the larger fetal pole) in the larger pole of the sac. This results in breech presentation, and thus cornual-fundal implantation of the placenta, it is concluded, is the principal cause of breech presentation in single, term pregnancies.

unless it can be flexed. If there is frank breech presentation and the legs are extended and the breech engaged, even though disengagement of the breech can be accomplished, the extended legs may so effectively splint the fetal trunk and spine as to prevent flexion of the fetus to a degree sufficient to permit successful external version.[11] As term approaches, the uterus tends to become more tense because it is stretched out further,[30] the fetus increases in size, and the abdominal wall is more tensely stretched, and thus, after the thirty-sixth week, it becomes generally more and more difficult successfully to perform external version. This is chiefly the case in primiparas, less and less so in increasing degrees of multiparity. A tense abdominal wall or an irritable uterus frequently may be initial causes for failure of the maneuver.

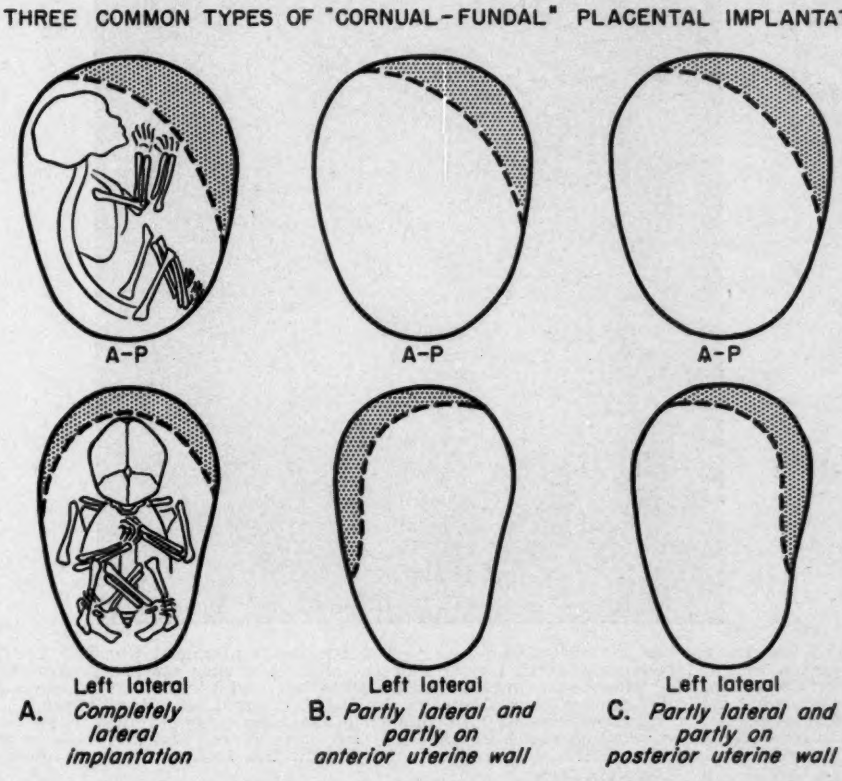

Fig. 4.—The above sketches are adapted from soft-tissue placentography x-ray films and show anteroposterior (top row) and left lateral (lower row) views of the term uterus. The three common types of *left* cornual-fundal placental implantation are pictured. When the placenta is in the right cornu, the anteroposterior views would picture the mirror images of the three figures on the top row, but the lateral views would be the same.

In Case "C" it is readily apparent that little or no placenta is implanted over the anterior wall of the uterus, and that external version could be performed with small chance of traumatizing the placenta. In Case "B," however, the opposite is true and the placenta might well be traumatized unless it is carefully avoided in carrying out the necessary manipulations of the fetal poles. In Case "A" the chance of causing some placental separation lies somewhere between these two extremes.

Procedure

We have found it helpful to explain briefly to the patient what we are about to do, simply stating that it will be better for her and the baby if we can "turn it around" so that the head is presenting instead of the breech. This nearly always gains her cooperation and sincere efforts at relaxation. The pa-

tient empties her bladder and then lies on her back on a flat table with a pillow under her head and the upper part of her shoulders, so as to flex her body slightly and thus take tension off the rectus abdominis muscles. Another pillow is placed under her knees, which permits slight flexion of the thighs and makes the patient more comfortable and relaxed. The aid of an assistant will seldom be necessary, and the office nurse can well serve in this capacity after a little instruction, should occasion arise. Such an occasion would usually consist of having one fetal pole held in a certain position while the operator uses both hands in carefully maneuvering the other pole past a narrow diameter of the amniotic cavity (see Step 3, Fig. 6).

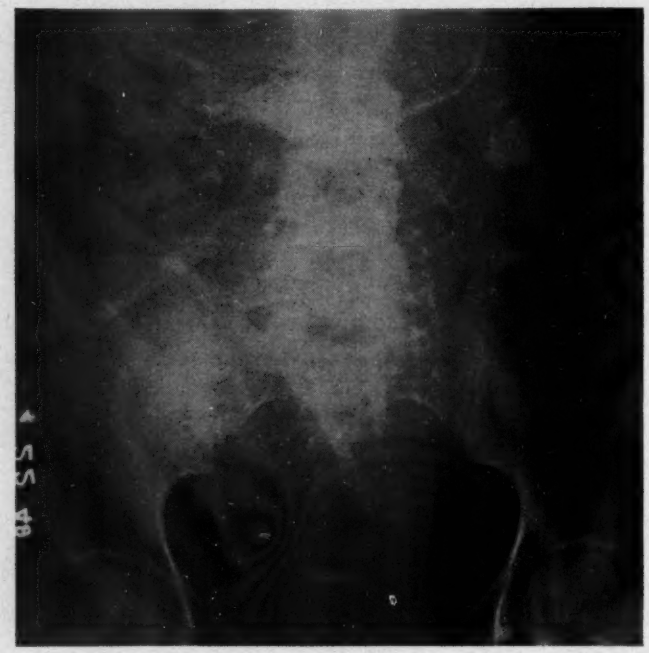

Fig. 5.—Anteroposterior soft-tissue x-ray of a near-term pregnant uterus. The placenta is implanted in the left cornual-fundal region of the uterus, mostly on the posterior wall, as in Case "C" of Fig. 4. There is frank breech presentation and the breech is engaged. This is the "extended attitude" of the fetus, described by Gibberd,[11] and later by Vartan.[33] In order to perform external version successfully in this case the breech would first have to be disengaged from the pelvis and brought up into the left iliac fossa, and the head would have to be moved in a counterclockwise direction until it and the spine were well flexed (as in Fig. 3).

Talcum powder applied generously to the patient's abdomen permits a more accurate application of pressure to the fetal poles and prevents the operator's hands from sticking to the patient's skin, which is particularly prone to occur in warm weather. The manual pressure applied to a fetal pole should be firmly and steadily applied and should be gentle; the sudden and jerky application of pressure may be dangerous. Pressure should be applied by the flat of the hand, not by one or two fingers. Before starting to turn the fetus, we auscult the fetal heart and note its rate and position; as soon as we have completed the version we check the fetal heart at once and if, after about 30 to 60 seconds, it is abnormal in any way we return the fetus to its original position, by reverse maneuver, and attempt the version again later on.

The method of performing external cephalic version which we recommend (Fig. 6) is, in general, similar to that commonly practiced except that we never

knowingly grasp or apply pressure to any fetal part when it lies against any portion of the placenta, which is to say that *we do not attempt to handle any fetal part if any of the placenta lies between our hand and that part.* In that way there is practically no chance of injuring the placenta during external version. The method used when the fetus has its back to the placenta is shown in Fig. 6; in this situation the fetus is usually fairly well flexed and the maneuver is more likely to be successful. When the fetus faces the placenta it is liable to have a somewhat less flexed attitude and external version may not be easily or successfully performed; our method in such cases is pictured in Fig. 7.

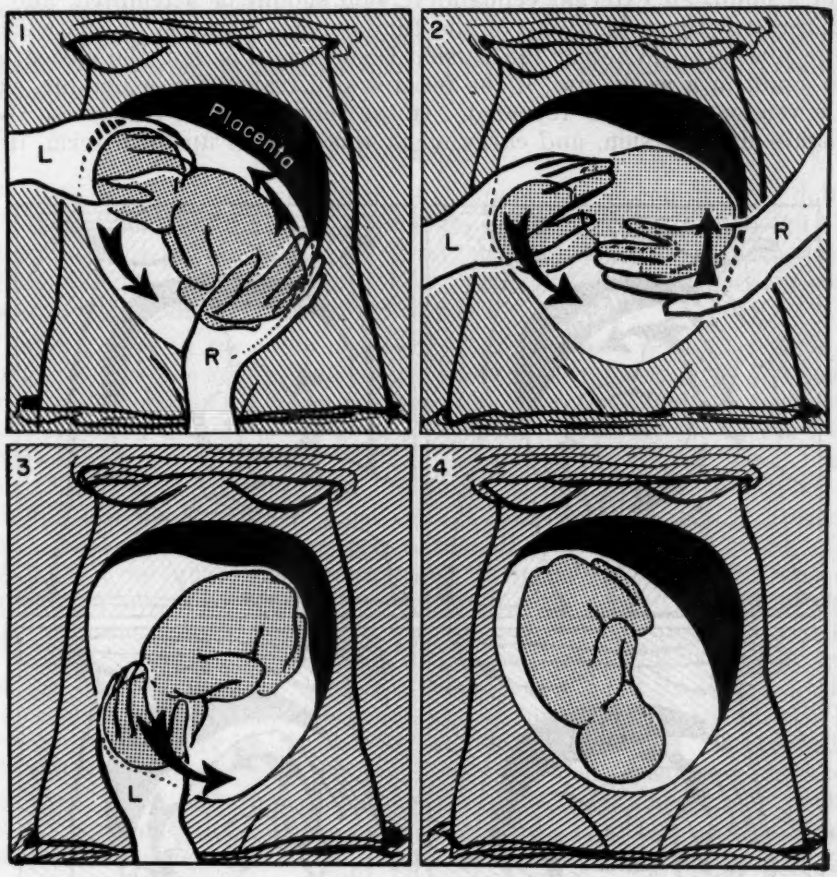

Fig. 6.—External cephalic version, as performed when the fetus lies in a left sacrum position and the placenta is implanted in the *left* cornu of the uterus. *Step 1:* The operator lifts the breech up out of the pelvic inlet with his right hand while he moves the head downward in a counterclockwise direction with his left hand. If the breech is engaged it should first be dislodged before the head is maneuvered. *Step 2:* The breech is moved upward until it disappears under the lower lateral border of the placenta. When this is achieved the hand is moved no higher but is held there in order to prevent the return of the breech to the lower left quadrant of the uterus. At the same time the head is maneuvered downward, in the direction of the arrow. *Step 3:* The head is brought on down toward the pelvic inlet, and as this is done the breech swings across the fetal surface of the placenta. *Step 4:* Version completed. The version has been performed in a manner which minimizes the chance of traumatizing the placenta since due care has been exercised not to handle any fetal part when any portion of the placenta lies between it and the operator's hand.

In external version there is much less chance of damaging the placenta (Fig. 4) if it lies mostly on the posterior wall of the fundus, and such danger is relatively great when it lies more in the anterior part.

External Version in Transverse Presentation

In any case in which transverse presentation of the fetus is found during or after the thirty-second week, x-ray placentography studies should be made at once, because 27 per cent, or 14, of our series of 52 cases of transverse presentation had placenta previa.[1] The following of this simple rule at the Boston Lying-in Hospital has permitted the discovery of 20 per cent of their cases of placenta previa before any vaginal bleeding has occurred.[1] If there is no evidence of placenta previa, the placenta, as we have shown, probably lies chiefly in the fundus of the uterus. With this characteristic placental position in the operator's mind, an external cephalic version should be attempted, and it can be performed without handling of the fundal portion of the uterus which contains the placenta. Whether the version is successful or not, the patient should be seen again in a week, and, if the fetus is still transverse or oblique, external cephalic version should be repeated. If the fetus is again transverse the next week, again do a version, and carry on in this fashion up until term, if neces-

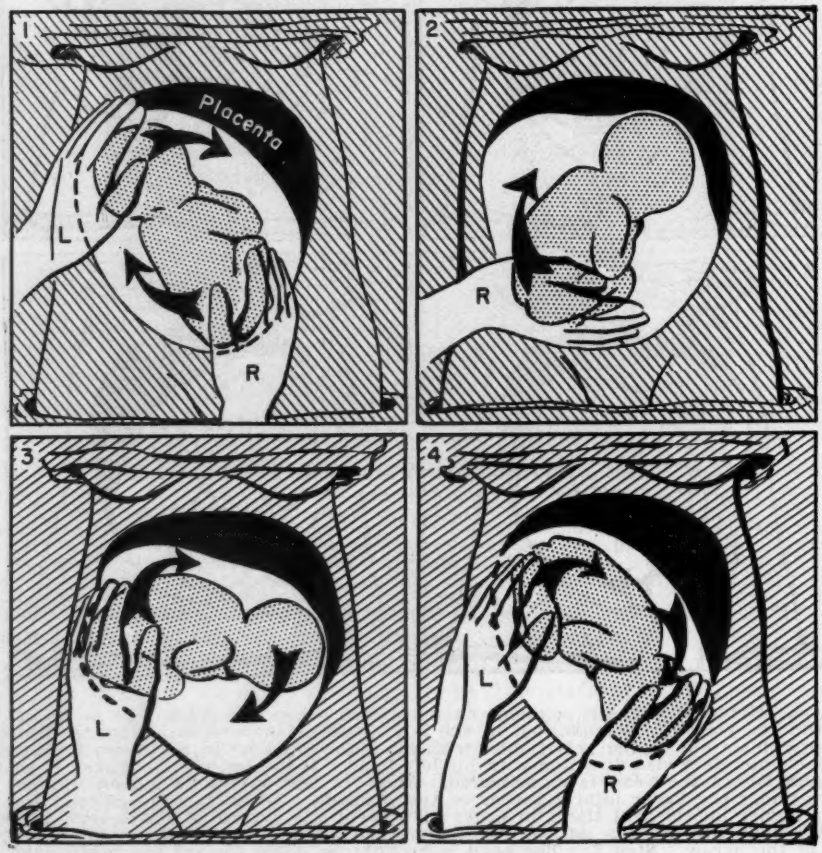

Fig. 7.—External cephalic version, as performed when the fetus lies in a right sacrum position and the placenta is implanted in the *left* cornu of the uterus. *Step 1:* The fetal head is pushed in a clockwise direction under the edge of the placenta and the breech is dislodged from the region of the pelvic inlet and moved, with the right hand, in a clockwise direction. *Step 2:* The breech is moved upward, causing the fetal head to swing to the left across the fetal surface of the placenta. *Step 3:* The breech is moved up into the right cornual region. *Step 4:* The head is picked up by the operator's right hand as it emerges from under the lower border of the placenta and is placed down over the pelvic inlet. If one's efforts to turn a fetus in the direction in which it is facing are unsuccessful, it may well be possible to turn it in the opposite direction. If the placenta is implanted in the right cornual-fundal region a mirror image of this figure will show the method of performing version.

sary, in order to insure that the patient goes into labor with the head presenting. The following of such a routine in handling the 52 cases of transverse or oblique presentation we reported[1] made it possible for 27 of them to be presenting cephalically at the time of onset of labor or at delivery, while 6 presented by the breech; 34 of these women were delivered through the vagina and the others by section, which gives an incidence of cesarean section in this series of 35 per cent. We agree with Garber and Ware[31] that the increased use of section and the decreased use of internal podalic version in the management of those unfortunate cases in which the patient has gone into labor with the fetus presenting transversely will decrease maternal and fetal mortality. In only one case in our series[1] was section necessary because of the onset of labor with subsequent incarcerated transverse presentation, and in no case was delivery accomplished by internal podalic version. There was no maternal mortality and 79 per cent of the infants survived.

Comment

We believe, thus, that the principal danger one encounters in doing external version, namely traumatic separation of the placenta, can be eliminated by determining in advance the placental implantation site in each case and by strictly avoiding the handling of that portion of the uterus which contains the placenta while manipulating the fetal poles.

What happens to the umbilical cord when external version is performed? It is probable that the same thing occurs when external version is done as when the fetus undergoes spontaneous version from breech to cephalic presentation. Weisman[32] showed that 24 per cent of all fetuses present by the breech at about 20 weeks of pregnancy. By 28 to 30 weeks only 8 per cent are still breeches, and about 6 to 7 per cent are presenting by the breech at 34 weeks. By 36 weeks, according to our figures,[2] about 4 per cent of fetuses still remain in breech presentation. This means, by simple calculation, that in any large group of pregnant women, who carry their pregnancies to term, about 21 per cent of the fetuses will undergo spontaneous version during the second half of pregnancy, and Vartan[33] shows that most of this occurs between the thirtieth and thirty-fourth weeks. A normal incidence of 23 per cent for a loop of cord around the neck of the fetus at the time of delivery has been quoted by Ryder,[16] which is about the same as the apparent frequency of spontaneous version. Whether there is any relationship between these two occurrences is problematical. Ryder[16] showed, however, that the incidence of a loop of cord around the neck in cases upon which external cephalic version had been successfully performed was 32 per cent, and thus, in his series of patients, external version appears to increase the occurrence of this condition beyond the normal average by one-third.

Our studies[1] have shown, in cases with fundal implantation of the placenta, that a loop of cord around the neck of the fetus, when there is cephalic presentation and labor is in progress, can fatally strangle the fetus in an appreciable proportion of instances. We had such fetal death in 2 of our 18 cases of this type. The situation is one in which the umbilical cord has to extend from the placenta in the fundus down around the fetal neck in the pelvic birth canal and back up to the umbilicus. A cord appreciably shorter than the average length of 55 cm.[34] would be drawn taut around the fetal neck as the head descends to the perineum, in cases in which this particular trio of conditions is fulfilled, and the hazard, though rare, is a real one. Almost the same situation may exist in patients who have had successful external version of a persistent breech to cephalic presentation, since again the placenta is situated almost as high in the fundus. By the same token, in breech delivery at term, if a loop of cord lies

between the fetal legs in the crotch it may become taut as the breech descends to the perineum and there may be some interference at least with the return of blood through the umbilical vein. In any case of this general type, if there is any degree of failure of fetal heart sounds during the latter part of labor a tight loop of cord around the fetal neck (when presentation is cephalic) or in its crotch (in breech presentation) should be suspected, and, if the cervix is fully dilated, intervention from below should be considered. In any case of breech presentation, of course, especially if it is not the frank type, one would much more frequently expect to find a prolapsed cord when there is some unfavorable alteration in the fetal heart sounds.

Finally, we would like to consider the optimum time in pregnancy at which external version should be done. In cases of persistent transverse or oblique presentation, when placenta previa has been ruled out, we believe that cephalic version should be done at from 32 to 34 weeks of pregnancy and repeated each week thereafter until term, if necessary. All women upon whom external version has been successfully performed should be palpated every week thereafter in order to detect and correct reversions. In our series of 52 cases of transverse presentation[1] 52 per cent came to delivery with cephalic presentation, and we believe that this was chiefly the result of the persistent efforts we directed toward achieving and maintaining cephalic presentation by external version. We believe the same general rule should be followed in cases of breech presentation. Ryder[16] has done most of his versions between the twenty-fourth and thirty-second weeks, and his chief reason for so doing seems to have been the ease with which it is done during this period. Our objection to this is that all but about 4 per cent of the cases will have undergone spontaneous cephalic version by 34 weeks, so many of his versions were done needlessly. Engagement of the fetal breech may occur fairly early in the primigravid woman, and this is even more true if it is a frank breech. For this reason we believe, in the primigravid woman, that the first attempt at external version should be made at 32 weeks of pregnancy and not postponed beyond 34 weeks, especially if less than an average amount of amniotic fluid is present.

As term approaches, the uterus in primigravidas more than in multiparas becomes more tense due to increased stretching[30] as the fetus enlarges, and one must, in general, exert more force in accomplishing external version. It becomes increasingly difficult to dislodge an engaged breech as term approaches, and failure to accomplish such disengagement is the most common cause of failed version. Just as readily, in general, as a successfully turned fetus can spontaneously revert to breech presentation can the operator successfully repeat external cephalic version, and this should be repeated as often as necessary in order to insure cephalic presentation at the time of onset of labor. Spontaneous reversion to breech presentation after 36 weeks of pregnancy, in our experience, is relatively rare, and usually occurs only in multiparas.

An important point our knowledge of the characteristic placental sites in breech presentation has taught us is that it may be very difficult to perform external version successfully when the placenta (Fig. 4) is implanted partly in the cornual-fundal region and partly on the anterior wall of the fundus on that side. The main difficulty in such cases is that so much of the anterior wall of the upper portion of the uterus on one side is covered by the placenta that our manual efforts are precluded over a relatively large portion of the maneuvering field. Conversely, when the placenta lies in the cornual-fundal region over the posterior portion of the fundus on that side, external version is generally accomplished with relative ease. When the placenta is implanted directly lateral to the cornual portion of the uterus the version is usually done without the application of any appreciable force, but in a few cases the breech seems to

move up next to the placenta and there to meet an impasse beyond which it cannot readily be made to progress, and we then cease our efforts without further ado.

One wonders why external cephalic version is not more widely practiced in the management of breech and transverse presentation of the fetus. We believe that it should be done in practically all cases, and should, without question, be performed in those cases of breech presentation in which slight inadequacy of the pelvic canal capacity for the after-coming head is suspected. A successful cephalic version, under these circumstances, permits the patient to have a test of labor, and she will deliver from below in a majority of cases, having a section, of course, if the degree of cephalopelvic disproportion appears to be too great. Since it is questionable whether there is any such thing as a relatively safe test of labor in breech presentation, external cephalic version will eliminate many of the sections which otherwise would have to be performed. The danger to mother and fetus incurred by the performance of external version, as we have outlined it, is very slight indeed, and is much less than that of breech delivery.

Summary

1. We have presented the underlying causal mechanisms of persistent breech and transverse presentations of the fetus in single pregnancies at or near term.

2. We recommend, in applying this knowledge clinically, that the implantation site of the placenta be determined in all cases of breech and transverse presentations of the fetus persisting after 30 to 32 weeks of pregnancy.

3. The knowledge of where the placenta is implanted is of great aid when one is performing external cephalic version, since this permits the manipulation of the fetal poles without handling that portion of the uterus in which the placenta is implanted, and thus the risk of traumatic placental separation (which is the one dangerous accident that may occur during the performance of external version) may be obviated.

4. In primigravid women in whom any degree of cephalopelvic disproportion is suspected, the conversion of breech presentation to a cephalic one will permit a test of labor and may obviate the necessity of section.

5. A general method of external cephalic version is pictured and described, and the performance of this valuable maneuver is recommended in the routine management of persistent transverse presentation because it permits delivery through the birth canal in two-thirds of these cases. It should also be performed on all patients with breech presentation persisting after 32 to 34 weeks of pregnancy so as to obviate the two to three times increased risk to the fetus which is attendant upon breech delivery throughout the country as a whole.

6. The optimum time for the initial performance of external cephalic version is about 34 weeks of pregnancy, in general, although nulliparous patients had best have their fetuses turned first at about 32 weeks. Engagement of the breech occurs fairly early in primigravid women, and disengagement of the breech becomes increasingly difficult as term approaches. Failure to disengage the breech is the most common cause of failed version.

7. Unfavorable accidents involving the umbilical cord resulting from external version are very rare. The fetal heart should be carefully ausculted before and just after performance of version, and if, after 30 to 60 seconds, it is not normal the fetus should at once be returned, by reverse maneuver, to its original position.

8. Anatomic factors which in general make the performance of external cephalic version difficult or impossible are: primigravidity, frank breech with extended legs, deep engagement of the breech, oligohydramnios, "extended attitude" of the fetus, and elongation of the amniotic sac resulting from relatively low implantation of the placenta in the cornual region it principally occupies. When external version cannot readily be accomplished, even though the breech has been successfully disengaged from the pelvic canal, it is probably because the placenta is offering mechanical blockage to the swinging past it of a pole of the fetus. Since the main precaution is to avoid placental separation, one should be willing not to attempt to force such a situation and should abandon the attempt for the time being. About one-fourth of such patients will undergo spontaneous cephalic version within the next week, but if this has not occurred, version should again be attempted, because it may then, surprisingly enough, be successfully performed with ease.

9. Since external cephalic version is an extremely safe and valuable obstetric maneuver, and one which any physician familiar with obstetric practice can easily teach himself to do, it is hoped that it will enjoy increased and widespread usage.

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A STUDY OF SERUM TRYPSIN INHIBITOR IN PREGNANCY

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THE facts and arguments suggesting the possible role of blood coagulative or fibrinolytic enzyme systems in the toxemias of pregnancy were assembled in an earlier publication from this laboratory.[3] It was also shown in that article that the interesting speculation by Schneider that toxemia of pregnancy was the result of placental thromboplastin entering the maternal circulation could not be supported by therapeutic tests. This article describes experiments which were devised to examine the possible role of the fibrinolysin enzyme system in pregnancy.

Quantitative Study of the Fibrinolysin Enzyme System

First, it is pertinent to review the quantitative methods used by others in studying the fibrinolysin enzyme system. Todd[19, 20] made quantitative measurements of the change in total fibrinolysin and antifibrinolysin in relation to streptococcal diseases and rheumatic fever. He used azocoll, an azo dye combination of collagen, as a substrate. Azocoll is broken down by proteolytic enzymes, and a deep red color results from the release of the azo dye. The amount of color released is proportional to the proteolytic activity. The concentration of fibrinolysin was determined in the serum after complete activation with streptokinase, while the inhibitor concentration was estimated by the inhibiting action of serum upon the digestion of azocoll by crystalline trypsin. Todd found that changes in fibrinolysin and antifibrinolysin titers in the same individual were not necessarily reciprocal.

Guest and associates[7] have devised a method for determination of antifibrinolysin using a bovine fibrinolysin preparation. It is, basically, the determination of the effect of serum upon the time required for a standard amount of fibrinolysin to dissolve a standard fibrin clot. According to their study the logarithm of the time required to dissolve the clot is inversely proportional to the logarithm of the fibrinolysin concentration. The relationship is a straight line function. By this technique they[8] found an increased antifibrinolysin activity in pernicious anemia, pneumonia, intestinal obstruction, acute bacterial endocarditis, and coronary thrombosis.

Christensen[4] studied all of the known components of the fibrinolysin system in normal controls and in a few diseased states. He used a modification of the fibrinogenolytic test first described by Ferguson.[5, 6] This test consisted of the inhibition of a standard digestive system composed of crystalline trypsin and bovine fibrinogen by various dilutions of the test serum. The system was standardized with crystalline soybean trypsin inhibitor. The degree of inhibition of fibrinogenolysis was determined by the lowest dilution of serum

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which permitted a clot to form after the addition of hemostatic globulin. Thus, since the inhibiting action of serum was tested on the proteolytic activity of trypsin rather than fibrinolysin, Christensen as well as Todd was more specifically measuring serum trypsin inhibitor titers. Christensen[4] also compared the fibrinogenolytic method he used with a spectrophotometric method used by Kunitz.[10] The results on testing three different sera using both methods gave comparable titers. In his clinical studies, Christensen found an increase in antifibrinolysin or serum trypsin inhibitor in cancer and other wasting diseases.

Study of Serum Trypsin Inhibitor

The various clot-lysis methods for the estimation of antifibrinolysin or serum trypsin inhibitor have the disadvantage of not demonstrating the intermediary effects of the process. We adapted the Kunitz[10] spectrophotometric method for our work, because with it we could study the reaction at various dilutions. Basically, this method consists in the estimation of residual proteolytic activity of a known trypsin solution acting upon a protein substrate after partial inhibition of the enzyme by serum. Since no adequately purified form of fibrinolysin was available to us, we selected crystalline trypsin as the proteolytic enzyme of reference because it was stable, and easily standardized. Both crystalline trypsin and fibrinolysin combine with antifibrinolysin, but this action by the enzymes is probably not qualitatively and quantitatively identical[4]; therefore, until we know what these differences are, this technique serves for the measurement of serum trypsin inhibitor only.

It was shown by Kunitz[11] and Schmitz[15] that isolated inhibitors, whether from soybean or pancreas, inhibit trypsin by combining with it in a mol to mol ratio to form an inactive trypsin-inhibitor compound which can be resolved again into its basic components. Schmitz[14] also demonstrated that when the "pancreatic inhibitor" was isolated from the plasma, it behaved in exactly the same fashion as that isolated from the pancreas. Surprisingly, when plasma itself was used, inhibition of trypsin was found to vary with the concentration of plasma, of added trypsin, or with the degree of dilution. This characteristic behavior had been previously observed by Hussey and Northrop[6] who found that the reaction was a reversible one which appeared to obey the mass action law. Thus,

$$\text{Inhibitor plus Trypsin} \leftrightarrow \text{Trypsin-inhibitor}$$

On this assumption and the further assumption that the two substances combine in an equimolar ratio, they derived an equation which conformed with their experimental reaction properties.

Our experience is similar. Curve *a* of Fig. 1 is a plot of the residual tryptic activity when the proteolytic action of trypsin upon casein is inhibited with increasing volumes of serum. This curve may be compared with curve *b*, also in Fig. 1, which was derived from the residual tryptic activity reported by Kunitz[10] when this trypsin system was inhibited with increasing amounts of crystalline soybean inhibitor rather than serum.

If these data (curve *a* from Fig. 1) are recalculated to determine specific inhibitory activity, that is by adjustment to standard volume, the resultant data, which measure the inhibitory activity, describe the straight line plotted in Fig. 2, curve *a*. If the data from Kunitz are similarly recalculated where soybean trypsin inhibitor was used instead of serum, curve *b* in Fig. 2 is found.

From curve *a* in Fig. 2, it is apparent that inhibitor activity is maximal at infinite dilution. Since the data appear to fall on a straight line, the intercept of this line upon the ordinate determines the specific inhibitory activity

at infinite dilution. The extrapolated value thus obtained is a comparable measure of specific inhibitory activity and it is this number which we have adopted for quantitative comparison of trypsin inhibitor titers. The trypsin inhibitor titer is expressed in inhibitor units for each 100 ml. of serum for one minute of digestion.

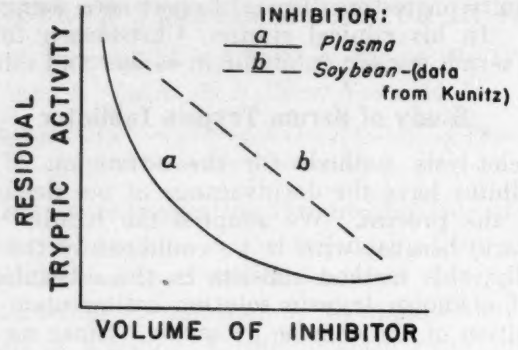

Fig. 1.

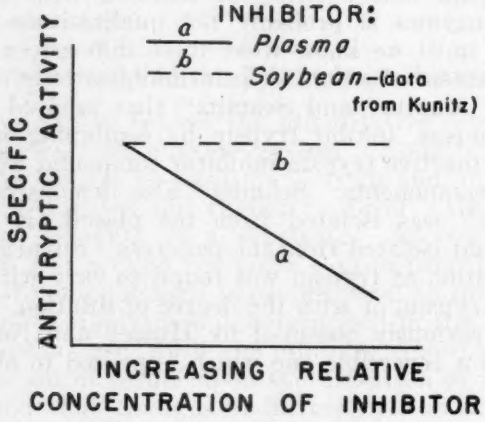

Fig. 2.

Occasionally there are encountered specimens for which the analytical data do not yield a straight line when plotted. There is a "break" in the curve. A thorough analysis of these atypical systems would require determinations at a number of dilutions, a procedure which is not feasible by the spectrophotometric method. These analytical "breaks" are definitely outside of the error of the method and require explanation. It might be that these systems indicate the presence of more than one inhibitor, or possibly suggest a change in the type of bonding. Fig. 3 is plotted from the data of a case which gave an atypical curve. It may be compared with Fig. 4, a "normal" curve.

Method

Tryptic activity or residual tryptic activity can be measured by the digestive action of crystalline trypsin upon casein. The amino acids liberated are measured according to the method of Kunitz[10] employing ultraviolet absorption. Since hydrolysis of casein by trypsin is not directly proportional to tryptic concentration, it is first necessary to construct a standard reference curve.

The trypsin standard curve is prepared as follows: Twenty-five mg. of crystalline trypsin are dissolved in 100 ml. of 0.0025 M hydrochloric acid. Samples varying from 0.1 to 1.0 ml. (0.025 to 0.25 mg.) of trypsin are pipetted into test tubes and each volume is adjusted to 2.0 ml. with saline. These tubes are then placed in a water bath at 37° C. for about five minutes to allow tem-

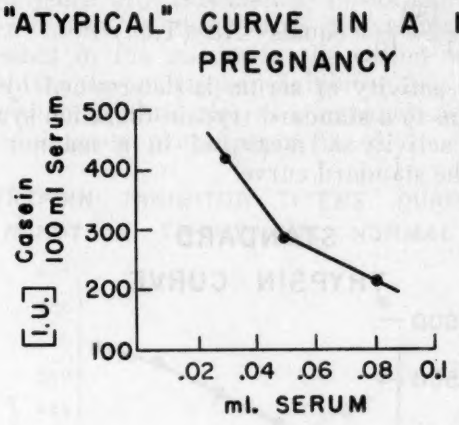

Fig. 3.

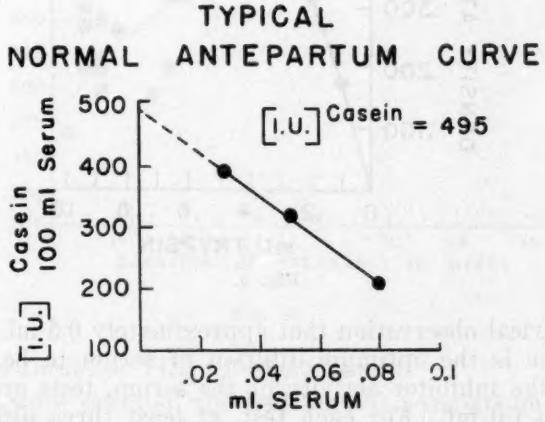

Fig. 4.

perature equilibration. One ml. of a 1.0 per cent solution of casein, according to Kunitz, is added at a convenient interval, about one minute, and the tubes are left in the bath for exactly 10 minutes. Three ml. of a 5 per cent solution of trichloracetic acid are then added to stop enzyme activity. The precipitate formed is centrifuged off after standing one hour at room temperature. The optical density of the supernatant fluid is measured in a Beckman spectrophotometer at 280 μ. The readings are corrected for the reagent blank. The amount of trypsin is plotted versus optical density to form the standard curve for the trypsin solution used. A typical standard trypsin curve is presented in Fig. 5.

A tryptic unit is defined by Kunitz[10] as the activity of trypsin which gives rise, under the conditions described, to an increase of one unit of optical density at 280 μ for each minute of digestion and is designated as (T.U.) Casein. Thus,

the specific activity of a sample of trypsin is obtained by taking the optical density for 0.1 ml. of trypsin and dividing by 10 minutes. For example, the trypsin solution used in the standard curve presented in Fig. 5 had an optical activity of .180 μ for 0.1 ml. of trypsin solution after 10 minutes of digestion. The specific activity of 1 ml. of this solution for one minute was equal to .18 $(T.U.)^{Cas.}$ or,

$$\frac{.180}{0.1 \times 10} \text{ equals } .18 \ (T.U.)^{Cas.}$$

The trypsin inhibitor activity of serum is determined by the addition of a suitable quantity of serum to a standard trypsin digestion system as described above. Residual tryptic activity is measured in a manner similar to that employed in determining the standard curve.

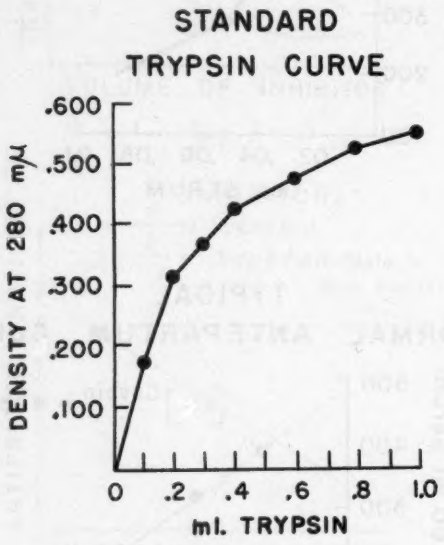

Fig. 5.

It is an empirical observation that approximately 0.5 ml. of a 1:10 dilution of serum in saline is the optimum dilution of serum to be used. Therefore, depending upon the inhibitor activity of the serum, tests are carried out over a range of 0.2 to 1.0 ml. For each test, at least three different dilutions of serum are used, and the resulting residual tryptic activity determined by reference to the standard trypsin curve. The difference between the residual tryptic activity so determined and the tryptic activity of the uninhibited sample (the standard trypsin curve) is the inhibitor value of the serum specimen tested. This value can be presented in inhibitor units $(I.U.)^{Cas.}$ One inhibitor unit is defined as the serum trypsin inhibitor activity required to inactivate one tryptic unit of Kunitz $(T.U.)^{Cas.}$

Results

Serum Trypsin Inhibitor Titers During Normal Pregnancy.—

Fasting venous blood samples were taken from twenty-two normal antepartum patients registered in the Sloane Hospital Clinic, and serum trypsin inhibitor levels were determined by the method described above. In twenty-one of these cases, determination of the inhibitor activity at three different dilutions gave data which when plotted, fell on a straight line. The one re-

maining case, which is not included, had a "break" in the curve which made it atypical. This case will be discussed separately later. The results of this study are presented graphically in Fig. 6. The ages varied from 22 to 34 years. There were eleven Negroes and ten white patients. Although the weeks of gestation, calculated from the day of the last menstrual period, varied from 11 to 37 weeks, the majority of the cases fell in the 12- to 20-week period. Our previous experience with this method in normal pregnant patients at term had always given values in the 500 to 600 range, and so we were, therefore, more interested in the results in the earlier weeks of pregnancy. The data showed that the serum trypsin inhibitor level varied from 360 to 630 inhibitor units with a gradual rise as pregnancy advanced. This increase is apparent when the data are plotted as in Fig. 6.

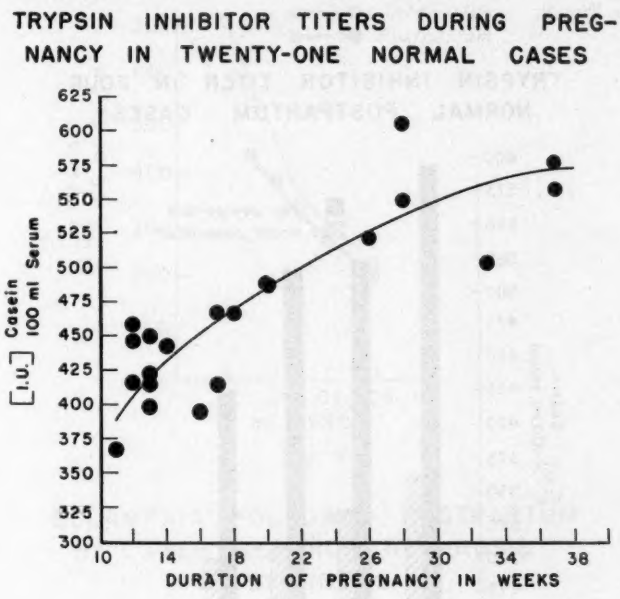

Fig. 6.

Serum Trypsin Inhibitor Titers Post Partum.—

Four patients were selected who had normal antepartum courses and who had uncomplicated labors and deliveries. Antifibrinolysin levels were determined in the fasting state one day post partum, and the test was repeated again one month post partum. The data are presented graphically in Fig. 7.

The average trypsin inhibitor value for the four cases one day post partum is 508 inhibitor units, for one month post partum, 323 inhibitor units.

Serum Trypsin Inhibitor Titers in a Case of Moderately Severe Pre-Eclampsia.—

A 28-year-old primiparous Negro was observed from the fourteenth week of pregnancy in the antepartum clinic. Her course was uneventful until the thirty-sixth week when she developed a swelling of the ankles, three plus proteinuria, and a rise in blood pressure to 135/85 mm. Hg. The patient was admitted to the hospital, but during the next seven days, in spite of bed rest, moderate sedation, and a low-salt diet, there was a progressive rise in the blood pressure which finally reached 185/90. The pregnancy was then terminated. This was accomplished by a cesarean section since there was definite cephalopelvic disproportion. Post partum, the toxemia gradually subsided, and

twelve days after delivery, when the patient left the hospital, the blood pressure was normal, the urine free of protein. A month later, the blood pressure was slightly elevated and there was a one-plus proteinuria.

Serum trypsin inhibitor titers were determined two days before delivery, the morning of operation, and twelve days post partum after the toxemia had largely subsided. When plotted, the two antepartum studies gave practically identical curves therefore, they are represented by a single "antepartum" curve in Fig. 8, which is an average of the two. This curve, as did each individual curve, had a "break" in it. It does not form a straight line and it is, therefore, not possible to extrapolate to the ordinate to determine the inhibitor level. After delivery, with clearance of the toxemia, the antifibrinolysin curve forms nearly a straight line, and there has been a decided drop in the inhibitor units at the lower dilutions studied. This change is represented by the "postpartum" curve in Fig. 8.

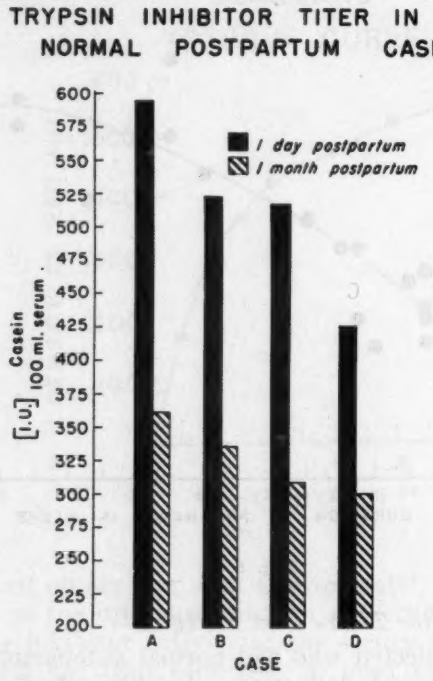

Fig. 7.

Serum Trypsin Inhibitor Titers in a Case of Eclampsia Complicated by Lower Nephron Nephrosis Syndrome.—

A 24-year-old Puerto Rican was followed in the clinic from the twenty-second week of her third pregnancy. Her first pregnancy terminated in an early abortion. Her second went to term, but it was complicated by hypertension and albuminuria in the last trimester. Her third pregnancy was essentially normal until the thirty-fourth week, when the patient was admitted to the hospital with a blood pressure of 200/120. The patient complained of pain in the epigastrium and tenderness over the liver area. The fetal heart could be heard. Six hours after admission, the patient became comatose and had a generalized convulsion. Fortunately, labor started spontaneously, and, after four hours, the patient was delivered of a living 2-pound infant. There were no more convulsions. During the first thirty hours in the hospital, a total of only 200 c.c. of urine was obtained. This oliguria persisted for the first three days post partum, then the urine output gradually increased, and after the seventh postpartum day, there was an adequate urinary excretion.

There were interesting alterations in blood chemistry which were due to the eclampsia and to the lower nephron nephrosis which followed. By the second postpartum day, the nonprotein nitrogen was 93.2 mg. per cent, the uric acid 7.6 mg. per cent, sodium 139 meq. per liter, and potassium 5.9 meq. per liter. Subsequently, the nonprotein nitrogen continued to rise until it reached 154 mg. per cent on the tenth postpartum day. The uric acid increased to 8.0 mg. per cent on the eighth postpartum day. The sodium dropped further and the potassium became more elevated, reaching 8.9 meq. per liter on the seventh postpartum day. With the restoration of a better urine output, the electrolytes and metabolites returned to nearly normal levels by the fourteenth postpartum day.

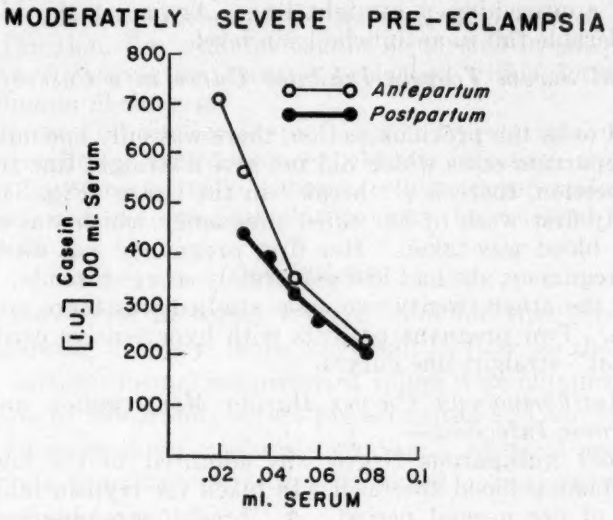

Fig. 8.

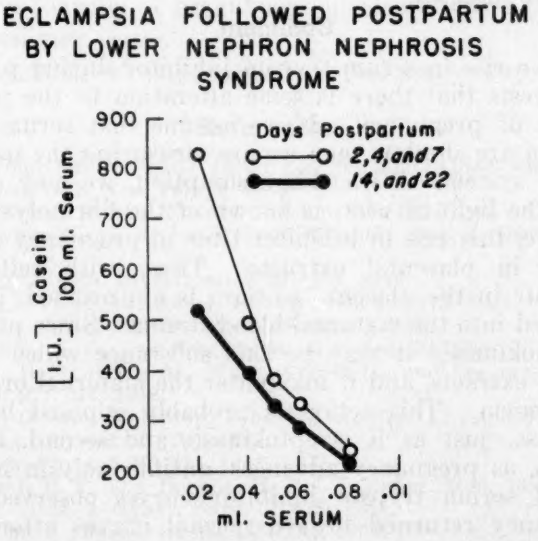

Fig. 9.

Serum trypsin inhibitor studies on this patient may be divided into two groups. The first group comprises the studies made on the second, fourth, and seventh days post partum while there was oliguria, hypertension, extensive electrolyte disturbance, and nitrogen retention. Included in the second group

are the studies made on the fourteenth and twenty-second days post partum, when the urine output was re-established, the blood pressure was more normal, the sodium and potassium were normal, and the nitrogen retention had been reduced. When the data for the studies in the first group are plotted, the curves are so close together that for practical purposes, in Fig. 9, they are represented by a thin-line curve which is an average of all three. There is a definite "break" in this curve just as was found in each individual study. The data from the two studies in the second group give practically identical curves and the average of these two curves is represented in Fig. 9 by a thick-line curve. With the clinical recovery of the patient, the curve becomes lower and straightens out approaching a straight line. Again, at the higher dilutions, there is a considerable fall in antifibrinolysin level.

An Atypical Serum Trypsin Inhibitor Curve in a Case of Normal Pregnancy.—

As referred to in the previous section, there was only one out of the twenty-two normal antepartum cases which did not give a straight line trypsin inhibitor curve. On inspection, there is a "break" in the curve (Fig. 3). This patient was in the thirty-first week of her third pregnancy which was entirely normal at the time the blood was taken. Her first pregnancy was essentially normal. In her second pregnancy, she had had moderately severe toxemia.

In none of the other twenty-two cases studied was there any previous history of toxemia. Two pregnant patients with hypertensive cardiovascular disease had "normal" straight line curves.

Atypical Antifibrinolysin Curves During Menstruation and in Cases of Cancer and Chronic Infection.—

A 26-year-old nulliparous Negro was admitted to the hospital for dysmenorrhea. A fasting blood specimen was taken for trypsin inhibitor study on the second day of her normal period. A "break" was observed in the curve.

Similar curves were found in a few patients with advanced cancer, syphilis, and chronic wasting diseases.

Comment

The progressive rise in serum trypsin inhibitor during pregnancy observed in this study suggests that there is some alteration in the proteolytic enzyme system as a result of pregnancy. If we assume that serum trypsin inhibitor and antifibrinolysin are similar, then we are measuring the inhibitor component of the fibrinolysin system. With this assumption, we may discuss the alterations observed in the light of what is known of the fibrinolysin system. Hypothetically, therefore, this rise in inhibitor titer in pregnancy may be due to the proteolytic factor in placental extracts. Thus, with cellular degenerative changes which occur in the placenta as term is approached, intracellular products may be released into the maternal blood stream. Since practically all tissue contains cytofibrinokinase,[2] it may be this substance which is the proteolytic factor in placental extracts, and it may enter the maternal organism to activate the fibrinolysin system. This action is probably opposed by, first, a specific anticytofibrinokinase, just as is streptokinase, and second, by a rise in antifibrinolysin. Thus, as pregnancy advances, antifibrinolysin increases.

The abnormal serum trypsin inhibitor curves observed in the cases of toxemia of pregnancy returned toward normal curves after the toxemia had subsided. This finding may be studied also hypothetically. A disturbance in placental function has been long considered to be the fundamental abnormality in toxemia of pregnancy. With the withdrawal of hormonal support from the uterus[16] and with the initiation of placental ischemia,[13] placental cellular degeneration would be greater than in normal pregnancy,[17, 18] and probably, as a result, the release and absorption of intracellular products would occur.

Again, cytofibrinokinase, probably released from these cells, may activate the fibrinolysin system which responds by increasing antifibrinolysin. Since there may be more than one type of profibrinolysin,[1] there may also be more than one type of fibrinolysin-antifibrinolysin complex. If these complexes have different rates of dissociation on dilution, this might explain the atypical curves we observed. Another possibility is that there is an alteration in the bond that holds fibrinolysin and antifibrinolysin, so that the rates of dissociation on dilution are not constant.

The alteration in blood coagulation referred to in the literature in toxemia and possibly in premature separation of the placenta may be related to this mechanism. For when activation of the fibrinolysin system is associated with impaired liver function, the inhibitor cannot be formed in adequate amounts.[12] Subsequently, blood coagulation becomes prolonged with failure of coagulation as fibrinolysin digests fibrinogen.

It is of interest that similar atypical serum trypsin inhibitor curves were found in other conditions such as cancer, chronic infection, and menstruation. These conditions have one factor in common, cellular degeneration. Thus, intracellular products such as cytofibrinokinase may be released to activate the fibrinolysin system.

Conclusions

1. A progressive rise in serum trypsin inhibitor titer was found during pregnancy. Following delivery, there was a fall in titer, so that, when studied one month post partum, normal nonpregnant values were obtained.

2. In one case of moderately severe pre-eclampsia and one case of eclampsia followed by a lower nephron nephrosis syndrome, atypical serum trypsin inhibitor curves were found which returned toward normal curves post partum with subsidence of the toxemia.

3. There is also the suggestion based on only a few cases that this aberration is found not only in toxemia of pregnancy but also in other conditions in which cellular degeneration may occur.

4. Possible physiological implications of this study were discussed.

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A STUDY OF THE MANAGEMENT OF PROLONGED LABOR*

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PROPER procedure in prolonged labor has merited lengthy discussion in standard obstetrical texts as well as in the literature. Eastman,[1] Schmitz,[2] Reid,[3] Calkins,[4] Murphy,[5] Cosgrove,[6] Siddall,[7] among others, who have approached the problem armed with the knowledge and experience of many years.

About ten years ago, Dr. David S. Hillis initiated a study of prolonged labor at Cook County Hospital which is still in progress. The present study was undertaken to stimulate early recognition of prolonged labor and to evolve a satisfactory plan of treatment.

Procedure

All cases of prolonged labor at the Cook County Hospital during 1947 and 1948 were divided into two groups: one was treated actively, as herein described, and the other was treated conservatively as "control patients." The latter method used as a "control" has been the accepted plan of care for prolonged labor at the Cook County Hospital. Because this conservative method often fails to terminate labor within a reasonable period and with satisfactory results, a more active form of treatment which would reduce fetal and maternal morbidity and mortality was sought.

Early in this study, it was necessary to define prolonged labor. Schmitz and associates,[2] in their study selected 24 hours, and Douglas and Stander[8] 30 hours as the period which must elapse before labor could be considered prolonged. Cosgrove and Glisson[6] state that the accepted average length of labor is 12 hours for multiparas and 18 hours for primiparas, but designated 36 hours as the period for onset of prolonged labor.

Peckham,[9] from 13,658 consecutive deliveries, calculated the average primiparous labor to be 16.57 hours in white patients and 17.66 hours in Negro patients, and 10.91 and 12.49 hours, respectively, for the two races among the multiparas.

In this study, a primiparous patient was considered to have a prolonged labor after 18 hours. The multiparous labor was considered to be prolonged after 12 hours.

Calculation as to the length of labor is dependent upon the criterion for the onset of labor. Whatever the criterion used, the determination of onset of labor varies with different clinicians on any one patient. The variation may involve many hours if palpation of cervical changes enters into the determination. Cervical changes are difficult to determine rectally, particularly in primary uterine inertia in which the cervical alterations occur slowly.

We are essentially in accord with Schmitz[2] in designating the onset of labor as that time when painful uterine contractions begin regardless of

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palpable cervical changes. We have designated the onset of labor to begin with the onset of painful uterine contractions which eventually result in palpable cervical changes. With this as the criterion, it was felt that the time of onset of labor would tend to be standardized for both series of patients.

Patients, on admission, are assigned in rotation to the services of the various attending surgeons of the obstetrical department. When prolonged labor was diagnosed and disproportion or other indications for special management were eliminated, they were automatically transferred to a special service for management. Patients in prolonged labor from three of the six attending services were treated actively, and those derived from the remaining three services were observed as controls. The patients throughout labor were under the direct management of the resident obstetrical staff supervised by the senior author who was consulted when any problem or abnormality arose.

Each patient in prolonged labor was examined vaginally with the use of strict aseptic technique. Effacement, dilatation, dilatability, and consistency of the cervix were determined. The presence of intact or ruptured membranes was noted. Diagnosis of the station, presentation, and position was also made. Particular attention was directed to the possibility of disproportion by evaluation of the size of the fetus and the type and adequacy of the pelvis. The Hillis impression method[10] was used routinely and x-ray pelvimetry was done when indicated.

Only full-term pregnant patients without other obstetrical or medical complications than prolonged labor were included in this study. Complications, such as disproportion, toxemias of pregnancy, bleeding, malpresentations such as breeches and transverse presentations were eliminated from the series. This was done because it was believed that such complications would interfere with the plan selected for care of these patients.

Following the vaginal examination, the patient received the therapy of the group to which she had automatically been assigned.

Active Management

The management of the active group was as follows:

1. The fetal membranes, if intact, were ruptured at the time of the vaginal examination.
2. The frequency, duration, and intensity of the uterine contractions were observed at the time of the vaginal examination. The uterine contractions of those patients whose membranes were artificially ruptured were re-evaluated one hour after the rupture.
3. If uterine inertia was diagnosed as determined by uterine contractions lasting less than 45 seconds, or if the intensity and frequency of the contractions was less than normally expected, posterior pituitary extract (Pitocin) was administered. Normal intensity of a uterine contraction was considered to be present when the uterine musculature resisted indentation by moderate pressure with a single finger (Calkins[4]).
4. If, with the establishment of normal uterine contractions for six to eight hours, satisfactory progress did not occur, the most satisfactory means for termination of the pregnancy was then decided upon.

The posterior pituitary extract was used in a diluted form in order to facilitate the administration of more accurate dosage and to prevent the accidental administration of an excessive amount. (One-half c.c. of posterior pituitary extract was diluted to 8 c.c. with sterile physiologic saline solution so that 1 c.c. of the mixture contained 1 minim of active substance.)

The posterior pituitary extract was administered subcutaneously by the medical staff only. The initial dose was ½ minim (0.5 c.c. of the mixture). The

effect of the first dose was observed very carefully. Its effect was used as an index of sensitivity of the uterus to the drug and governed subsequent doses to be administered. Repeated doses of posterior pituitary extract were given at twenty-minute intervals and the amount was gradually increased as indicated to 1 minim; then 1.5 minims; then 2 minims, and then 3 minims and upward in an attempt to establish uterine contractions of approximately 45 to 60 seconds' duration and of satisfactory intensity with good relaxation between contractions. Once the desired effect was obtained, this maintenance dose, varied as indicated by the uterine response, was administered at twenty-minute intervals until the rate of progress indicated the approach of the second stage. The fetal heart tones, maternal blood pressure, the length, frequency, and intensity of uterine contractions, and the adequacy of uterine relaxation between contractions was determined prior to the administration of each succeeding dose of posterior pituitary extract.

Inactive Management

The inactive management of control patients followed a plan of care previously in effect at the Cook County Hospital, and consisted of sedation in an attempt to allow alternating periods of rest and labor; adequate fluids and carbohydrate intake (either orally or intravenously); nursing care, including evacuation of the bowels and bladder; and constant observation for development and prevention of acidosis and maternal exhaustion. Operative interference was instituted when maternal or fetal indications were present.

Incidence

The number of cases of prolonged labor during the period studied was 598, or 3.9 per cent of the total deliveries.

Patients treated in the active series included 266 with prolonged labors, of whom 158 were primiparas and 108 multiparas. The inactive group included 290 with prolonged labors, of whom 192 were primiparas and 98 multiparas. Forty-two patients were not included in the statistics because of concurrent abnormalities.

Treatment

Of the total 266 cases treated in the active manner, there were 196 in which it was found that the membranes required artificial rupture at the time of the sterile vaginal examination (Table I). This procedure alone was all that was required to alter the character of the labor in 87 (44.4 per cent of the patients so treated) or 32.7 per cent of the total actively treated patients and no further therapy was required to effect delivery.

TABLE I. ACTIVE THERAPY

ACTIVE THERAPY	NO. CASES	PERCENTAGE
Artificial rupture of membranes	87	32.7
Artificial rupture of membranes plus Pitocin	109	41.0
Pitocin alone	59	22.2
No therapy required	11	4.1

Seventy patients (26.3 per cent of the total) were found to have ruptured membranes at the time of the vaginal examination. Of these, 11 (4.1 per cent of the total) had satisfactory uterine contractions so that stimulation was not required. These patients received no active therapy to effect their delivery. As for the remainder of the patients (168 patients or 63.1 per cent of the

total actively treated patients), the uterine contractions were deemed unsatisfactory. The uterine inertia of these patients was treated with injections of the posterior pituitary extract in dosages as described.

Of the patients receiving posterior pituitary extract (Table II), 45.8 per cent required individual doses of 1 minim or less for production of effective uterine contractions. An additional 45.3 per cent required 1½ to 3 minims. The uterine inertia was so great in 7 patients (4.2 per cent) that individual doses of over 4 minims of posterior pituitary extract (maximum of 8 minims) were required for production of satisfactory uterine contractions.

TABLE II. ADMINISTRATION OF POSTERIOR PITUITARY EXTRACT

MAXIMUM DOSE MINIMS	TOTAL	
	NO.	PERCENTAGE
1 or less	77	45.8
2	51	30.4
3	25	14.9
4	8	4.8
Over 4	7	4.2

Of the 15 patients receiving over 3 minims of posterior pituitary extract per dose, 5 were delivered by cesarean section and one by midforceps after Dührssen's incisions. The remainder had spontaneous deliveries or prophylactic outlet forceps. There were no fetal or maternal deaths in this group.

Results

Length of Labor. The average length of labor in the active group for primiparas was 25 hours, 35 minutes; for multiparas it was 17 hours, 25 minutes (Table III). In the inactive group the length of labor was 37 hours, 5 minutes for primiparas and 24 hours, 55 minutes for multiparas.

Thus, the average length of labor in the inactive group was 11 hours, 30 minutes longer in the primiparas and 7 hours, 30 minutes longer in the multiparas than in the active group.

TABLE III. AVERAGE LENGTH OF LABOR

SERIES	TOTAL CASES	PRIMIPARAS		MULTIPARAS	
		NUMBER	LENGTH	NUMBER	LENGTH
Active	266	158	25 hr. 35 min.	108	17 hr. 25 min.
Inactive	290	192	37 hr. 5 min.	98	24 hr. 55 min.

The length of labor after institution of therapy in the active series was 4 hours, 55 minutes for primiparas, and 2 hours, 25 minutes for multiparas. The fact that the labors were so promptly terminated in the actively treated patients, after the initiation of therapy, indicated that the total length of labor might have been even further reduced had the prolonged labor been recognized more promptly than it was in some instances.

Operative Deliveries.—The incidence of forceps deliveries was 30.75 per cent in the active series and 39.3 per cent in the inactive series (Table IV). The variation in the incidence of forceps deliveries in the two series was not significant, but the incidence of the deliveries other than low forceps was increased in the inactive series. The reduction in the incidence of midforceps deliveries in the active series is noteworthy (0.75 per cent as compared to 3.1 per cent in the inactive series). The reduction in midforceps deliveries and other operative deliveries (Dührssen's incisions and cesarean sections) was

also reported by Eastman[1] in a larger series of cases where posterior pituitary extract was used for uterine inertia.

TABLE IV. FORCEPS DELIVERIES

	ACTIVE SERIES						INACTIVE SERIES					
TYPE	NUMBER	INCIDENCE	MATERNAL MORBIDITY	MATERNAL MORTALITY	FETAL MORBIDITY	FETAL MORTALITY	NUMBER	INCIDENCE	MATERNAL MORBIDITY	MATERNAL MORTALITY	FETAL MORBIDITY	FETAL MORTALITY
Low	72	27.0%	1	0	0	1	79	27.2%	2	0	1	1
Mid	2	0.75%	0	0	0	0	9	3.1%	1	0	1	2
High	0	0	0	0	0	0	0	0	0	0	0	0
Rotations	8	3.0%	0	0	0	0	26	9.0%	1	0	0	0

Although Murphy,[11] in his study with the tocograph, suggests that the spontaneous rotation of the posterior occiput to the anterior position is not dependent upon the quality of the uterine contractions, the incidence of forceps rotations (key-in-lock or Scanzoni's maneuver) is 3.0 per cent in the active group as compared to 9.0 per cent in the inactive series.

There were eight cesarean sections (low cervical) in the active group (3.02 per cent). Seven of these were performed following posterior pituitary extract failure, and resulted in the delivery of living babies. Two of these failures were attributable to unrecognized disproportions, and three to the presence of constriction rings. Two other patients were delivered by cesarean section because of unsatisfactory progression of cervical dilation with posterior pituitary extract administration. The eighth cesarean section was performed on an elderly primipara who had received no Pitocin.

Other operative procedures in the active group included one Dührssen's incision, with a midforceps delivery done for fetal distress.

Three cesarean sections were done in the inactive group (1.0 per cent). One was done in the case of an elderly primipara, and the other in a primipara after 61 hours of labor with very poor progress. Another was done in a multipara after 40 hours of labor with little progress. Other operative procedures included two Dührssen's incisions and two craniotomies on dead babies (Table V).

TABLE V. OPERATIVE DELIVERIES, EXCLUDING FORCEPS

	ACTIVE SERIES					INACTIVE SERIES				
TYPE	NUMBER	MATERNAL MORBIDITY	MATERNAL MORTALITY	FETAL MORBIDITY	FETAL MORTALITY	NUMBER	MATERNAL MORBIDITY	MATERNAL MORTALITY	FETAL MORBIDITY	FETAL MORTALITY
Cesarean section	8	0	0	0	0	3	2	0	0	1
Dührssen's incision	2	0	0	0	0	2	1	0	0	1
Craniotomy (on dead babies)	0	0	0	0	0	2	0	0	0	2

The fact that there was a significantly smaller number of patients in the inactive series who were delivered by cesarean section may be at least partially explained by the prevailing attitude in prolonged labor of nonoperative interference.

Complications.—The occurrence of a constriction ring was recorded in four patients in the active series. All had received posterior pituitary extract. Three of these patients were delivered by cesarean section, while the fourth was delivered of a live fetus through the birth canal. Three patients

in the inactive series developed constriction rings. One fetus died in utero and a craniotomy was performed for delivery. The other patients were delivered vaginally of living babies.

Postpartum hemorrhages occurred in six patients (2.3 per cent) in the active group. One of these was attributable to a retained succenturiate lobe of the placenta. Postpartum hemorrhages occurred in eight patients (2.8 per cent) in the inactive group.

Other complications which occurred in the inactive group included a spontaneous amputation of the anterior lip of the cervix, and third-degree laceration of the perineum following a midforceps delivery.

The initial dose of ½ minim of posterior pituitary extract was deemed excessive in one instance, resulting in a moderate contraction, lasting two and one-half minutes; the patient was given ether for several minutes, and one-half hour later was given 1/10 minim of posterior pituitary extract which resulted in satisfactory uterine contractions adequate for a normal spontaneous delivery. After delivery, there was no indication of fetal injury.

Morbidity

The maternal morbidity, by the criteria of the Joint Committee on Maternal Welfare, in the active group consisted of three cases of endometritis, or an incidence of 1.1 per cent, which compares favorably with the corrected morbidity at our institution. The maternal morbidity in the inactive group was 4.3 per cent (corrected). This included 12 cases of endometritis, one of mastitis, and one of pulmonary atelectasis also included in the group with endometritis. In addition, there were 4 patients in the inactive group who had intrapartum sepsis; these patients received appropriate therapy and were not morbid post partum.

Twenty-one patients (7.9 per cent) in the active group and 59 patients (19.7 per cent) in the inactive group received either sulfadiazine or penicillin, or both, for prophylactic purposes or for treatment in the presence of sepsis.

Mortality

There was no maternal mortality in either group. There were two fetal deaths (an incidence of 0.75 per cent) in the active group. Both were of term infants born with several loops of cord tightly around the neck. Both mothers received posterior pituitary extract from which no abnormal contractions resulted. One newborn showed evidence of intracranial injury but recovered satisfactorily.

Thirteen fetal deaths (4.5 per cent) occurred in the inactive group, five neonatal and eight intranatal, including one set of twins. Two other newborn infants showed evidence of intracranial pathology but were discharged in apparently good condition.

Comment

Using the method of active therapy as described, we found that the prolonged labors were terminated in a definitely shorter period of time. The number of protracted labors was also decreased. This is shown by the fact that 6.4 per cent of the primiparas in the active group were in labor over 36 hours as compared to 36.4 per cent in the inactive group, and 0.9 per cent of the multiparas in the active group were in labor for over 36 hours as compared to 17.3 per cent in the inactive group (Figs. 1 and 2). Labors of over 36 hours in the active group occurred in these patients having primary uterine inertia where no palpable cervical changes were notable for many hours after the on-

set of painful uterine contractions. This inability to determine the presence of labor delayed the application of the active treatment and resulted in several labors of protracted duration. The greater incidence of protracted labors in the inactively treated series was naturally accompanied by increased maternal apprehension and exhaustion. These patients required larger quantities of sedation and fluids in an attempt to prevent acidosis. Comparative studies also indicated that the operative procedures, complications, maternal morbidity, and fetal mortality were appreciably reduced in the actively treated group.

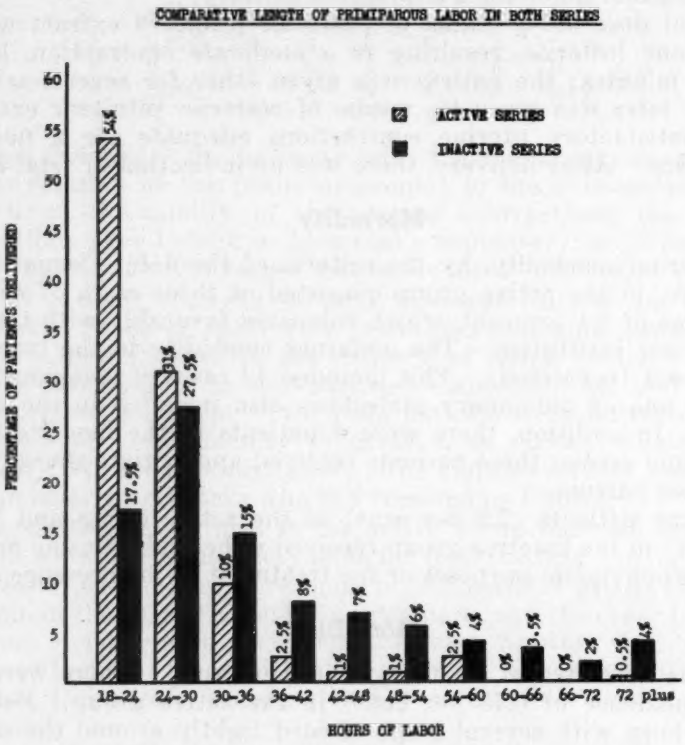

Fig. 1.

Those patients (2.6 per cent) who exhibited the severest type of uterine dysfunction complicated by constriction rings, inertia refractory to stimulation, cervical dystocia, and unrecognized disproportions were recognized earlier than in the inactive group, and appropriate surgical measures for delivery were taken while the mother and the baby were still in good condition, and within that period of time when a relatively safe operative delivery might be performed.

We believe, along with Schulze[12] and Greenhill,[13] that ruptured membranes do not retard, but promote the progress of labor as indicated by the successful termination of 32.7 per cent of the prolonged labors in the active series, in which artificial rupture of the fetal membranes resulted in increased uterine contractions, and a successful termination of labor with no additional stimulation. The increased danger of morbidity in the presence of ruptured membranes caused little concern since, with the active treatment, labor was terminated within a comparatively short period of time after the artificial rupture.

A possible disadvantage of rupture of the fetal membranes at this stage of labor is that one is committed to delivery within a reasonable period of time after such rupture. Experience has shown, however, that in reality this is an advantage, since those patients who do not deliver in a reasonable period of time after rupture of the membranes are those who have the severe type of uterine dysfunction as previously described. It is well to uncover such cases early in labor. The early recognition of these abnormalities accounts for the increased incidence of cesarean sections in the active group (3.0 per cent), although this incidence is still within satisfactory limits for prolonged labors.

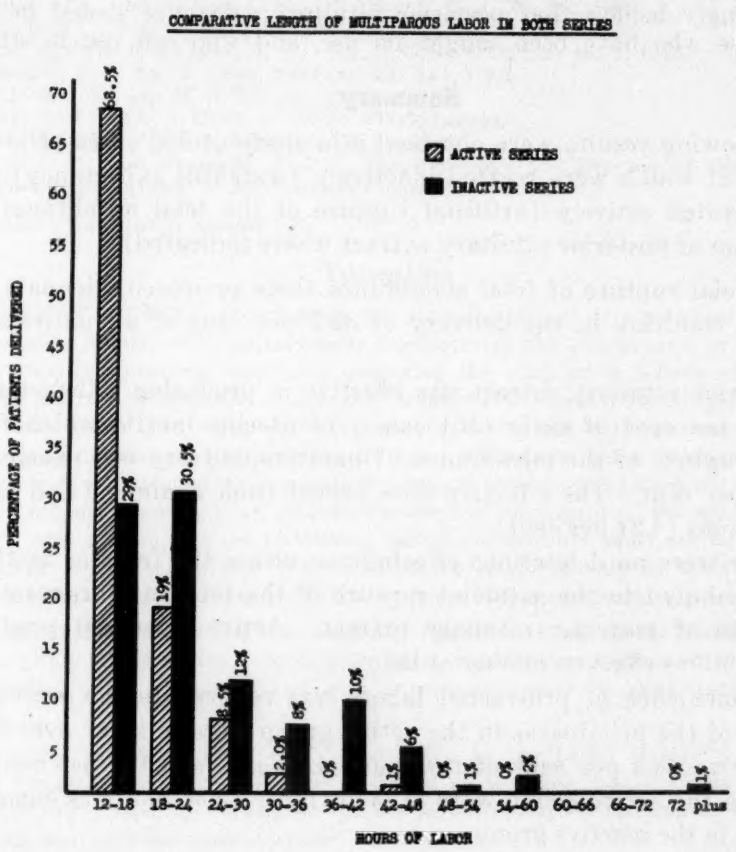

Fig. 2.

In addition to stimulation of uterine contractions, it had been noted previously that the presence of ruptured membranes also resulted in more satisfactory progress of labor when posterior pituitary substance was administered, and smaller doses of posterior pituitary substance were sufficient to overcome uterine inertia.

We encountered no complication attributable to the artificial rupture of the membranes. Perhaps the series of cases is too small to warrant such an optimistic attitude. Nevertheless, in our opinion, the advantages seem to outweigh any possible disadvantages.

We are well aware of the disrepute in which the use of posterior pituitary extract before the onset of the second stage of labor is held and its disastrous results when a preparation not accurately assayed is used. We know, how-

ever, of no other drug which would provide uterine stimulation in as satisfactory a manner. We feel that this is a naturally occurring hormone which can be specifically and physiologically utilized. At present it is fairly accurately assayed and relatively dependable. This is highly essential when dealing with an organ such as the laboring uterus, which varies in its response from patient to patient, and from time to time in the same patient.

We are also cognizant of the fact that the weight of obstetrical authority is opposed to the use of this drug in the first and second stages of labor. We feel, however, that so valuable a hormone should not be discarded but studied thoroughly for further evaluation of a safer method of administration.

We strongly believe that posterior pituitary substance should be utilized only by those who have been taught its use, and who can use it safely and cautiously.

Summary

The following results were obtained in a study of 556 cases of prolonged labors, part of which were treated inactively (watchful expectancy) and the remainder treated actively (artificial rupture of the fetal membranes and/or administration of posterior pituitary extract where indicated):

1. Artificial rupture of fetal membranes alone produced adequate uterine contractions resulting in the delivery of 32.7 per cent of all patients in the active series.

2. Posterior pituitary extract was effective in producing satisfactory progress in 95.8 per cent of cases (161 cases) of uterine inertia which failed to respond to rupture of the membranes. Operative delivery was deemed necessary in 4.2 per cent. The effective dose varied from 1 minim (45.8 per cent) to over 4 minims (4.27 per cent).

3. There were no deleterious effects upon either the fetus or mother that could be attributed to the artificial rupture of the fetal membranes or to the administration of posterior pituitary extract. Active treatment produced no obvious deleterious effect on mother or baby.

4. The incidence of protracted labors was reduced in the active series; 6.4 per cent of the primiparas in the active group were in labor over 36 hours as compared to 36.4 per cent of the inactive group, and 0.9 per cent of the multiparas in the active group were in labor for over 36 hours as compared to 17.3 per cent in the inactive group.

5. There was a distinct decrease in incidence of midforceps deliveries in the active series. The rate of cesarean section was higher in the active group (3.0 per cent to 1.0 per cent).

6. The rate of other operative procedures (Dührssen's incisions and craniotomies) was higher in the inactive series.

7. The incidence of maternal complications was greater in the inactive series than in the active series.

8. The maternal morbidity was 1.1 per cent in the active series as compared to 4.3 per cent (corrected) in the inactive series.

9. The fetal mortality was 0.75 per cent in the active series as compared to 4.5 per cent in the inactive series.

10. There were no maternal deaths in either series.

We wish to thank the other members of the Obstetrical Staff of the Cook County Hospital (Drs. James E. Fitzgerald, Alfred J. Kobak, Louis Rudolph,* Augusta Webster, and Charles Fields) for their cooperation in contributing their patients to this study.

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Discussion

DR. JANET TOWNE.—It is difficult for one to be critical of a presentation that shows such remarkable results. The authors have demonstrated the effectiveness of their management in vertex presentations, and have illustrated the value of a definite regime with all complicating factors eliminated. Since the primigravida constitutes 75 per cent of any prolonged labor series studied, an extremely careful evaluation of the patient must preclude rupturing the membranes or administering Pitocin. We believe that a fundamental factor in the production of a prolonged labor is disturbed muscle physiology. This is not so much a lack of pituitary stimulation as it is an inefficient myoneural coordination. Successful results may be obtained with Pitocin, but the underlying pathologic condition must not be ignored. The authors' point is well taken, that Pitocin should be employed only by those trained in its use, and that abuses are to be expected if there is a widespread return to general usage.

The maternal morbidity and fetal mortality figures as shown are the lowest on record for any similar group of cases. On a comparative basis, a parturient is better off with a prolonged labor at Cook County Hospital, than with a normal delivery at most institutions in the country.

Our recent prolonged labor study undertaken at the Lewis Maternity Hospital, the obstetrical teaching hospital for the Stritch School of Medicine, has shown us that increased dangers arise when labor is prolonged. In our series, a marked increase in fetal mortality and maternal morbidity has been observed.

The statistical survey presented further shows that six of the eleven cesarean sections were performed on patients who showed "unsatisfactory progress." Termination of prolonged labor by cearean section carries a very high maternal morbidity as shown by Williams in his analysis of 206 deaths in prolonged labor. We have not considered "unsatisfactory progress" as an indication for abdominal delivery. Instead, we contend that not only is the patient best served by conservative management, but conservatism is indicated by available facts.

DR. HENRY BUXBAUM.—I would like to comment on a few points. The authors' definition of the onset of labor based mostly on subjective signs seems to me to be indefinite and uncertain. I am sure you all have had experience with patients with regular rhythmic uterine contractions plus a low pain threshold, whose pains seemed severe enough to warrant sedation, who were discharged from the hospital twenty-four hours later as false alarms, only

*Deceased.

to return a week later and deliver spontaneously. I believe some objective signs should be present before a diagnosis of labor is made, such as a cervix that is starting to dilate and/or efface.

I heartily agree with the essayists that all patients with prolonged labor are entitled to a clean vaginal examination for re-evaluation. This includes the size and architecture of the pelvis and the position, station, and size of the occupant of the uterus, especially in relationship to the inlet of the pelvis. Also their advocacy of attempting to impress the head is of great prognostic significance. If the head can be impressed to the spines it will most likely deliver from below, if not we still can resort to a trial of labor.

In the active group they employed artificial rupture of the membranes with an incidence of 32 per cent success, and in the inactive group they resorted to sedation and hydration. What I at least can learn from the above statement is that a combination of both forms of therapy, i.e., rupture of membranes, hydration and sedation in any one given case may obviate the necessity for the use of oxytocics. To put it inversely, therefore, one should not use Pituitrin or Pitocin stimulation until after the membranes have been ruptured and the patient has had a period of rest. I agree with Drs. Daro and Gollin that Pituitrin is a highly potent drug and should be used very cautiously and sparingly especially with the child still in the uterus. Even in the best of hands under the closest supervision cases of uterine tetany and fetal distress have been reported.

Incidentally I am of the opinion that it is safer to give small doses of pituitrin intravenously over an extended period of time rather than intramuscularly. If 1 minim of Pitocin is put in 100 c.c. of solution, which is administered at the rate of 28 drops per minute, it will take one-half hour to give ½ minim of the drug. Therefore, there is no concentration of Pituitrin in the system at any one time and the pains initiated will more closely approximate the normal uterine contractions, and, last, at the first sign of danger the drug can be stopped instantly which is not possible when it is given intramuscularly.

Calling attention to Table IV, I would like to comment that if the newer classification of forceps is to be universally adopted, they will have to revise their number of midforceps upward, because in the active group they mentioned two midforceps, but had 8 rotations, and, as you are aware, cases in which rotation is required are automatically classified as midforceps. Therefore, in keeping with this newer teaching, in the inactive group, instead of 9 midforceps they had at least 26. Also, in their conclusions they stated that there was a higher rate of Dürhssens incisions in the inactive group which is not borne out in Table V.

I would like to call attention to the extremely low incidence of cesarean sections in this series of prolonged labor; and the fact that they never considered it necessary to resort to the extraperitoneal variety. In spite of which, they had an unusually low maternal morbidity and no maternal mortality .

DR. JAMES E. FITZGERALD.—I would like to clarify a few things about this paper, which I believe is quite worth while.

The inactive series Dr. Daro talked about is not the Cook County Hospital method. For the purpose of this paper part of the cases were put in the group where no treatment was used. This is not the accepted method by the rest of the Staff.

One other thing that I would like to point out is that our maternal morbidity is extremely difficult to evaluate. If patients deliver normally they are sent home on the third day and some on the second. I have an idea that whatever morbidity we have develops in the home and not in the hospital, so I do not think those figures are very accurate.

I would like to point out two things. One was Dr. Towne's figure on prolonged labor which seemed to be higher than should be necessary. I think there is apparently some room for interpretation in terms of prolonged labor. We do know that inactivity of the uterus is due to some neuromuscular pathology. If it responds to methods of treatment that allow the patients to deliver, I think that is worth while.

I always thought you should treat what is wrong with the patient. If she is bleeding, treat the bleeding. If she has high blood pressure, treat the high pressure. If you have a uterus that is functioning abnormally, you should attempt to treat that abnormal function. I think Dr. Daro tried to do it.

I would like to point out that a large percentage of patients with so-called prolonged labors deliver spontaneously without anything more active than rupture of the membranes. Another thing, a goodly proportion respond to a small dose of Pituitrin, which should be relatively harmless. On the other hand those patients in whom large doses of Pituitrin were necessary often responded poorly.

DR. DARO (closing).—Dr. Fitzgerald has given us part of the answer concerning our morbidity statistics. Another factor was that these were uncomplicated cases except for the number of hours of labor, therefore, our morbidity statistics would differ from studies such as Dr. Towne's, where all patients were included.

Regarding Dr. Buxbaum's discussion, I would like to say that we do not offer this form of treatment as a panacea. When we started this study, we were seeking a better method than expectancy alone. It seems to us that rupture of membranes and giving of adequate doses of Pituitrin bring good results.

A few words about Pituitrin. It is a natural substance and when used adequately will do good and no harm. The one case where ½ minim produced an undesirable response was interesting in that the optimum dose was found to be 1/10 minim of Pituitrin. I think that instead of condemning Pituitrin, we should condemn the use of improper doses of Pituitrin.

VAGINAL HYSTERECTOMY, THE TREATMENT OF CHOICE FOR BENIGN ENLARGEMENTS OF THE UTERUS*

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TO THE ever-increasing if not already too voluminous literature that has accumulated on the subject of vaginal hysterectomy, the authors wish to add their humble contribution of yet another series somewhat smaller than many others reported, yet large and all-inclusive enough to reach certain definite conclusions. Our series comprises 1,121 cases of vaginal hysterectomy alone and/or combined with other pelvic and vaginal plastic procedures. A moderate number of operators, mainly gynecologists, but also a few general surgeons, have performed these operations at Mount Sinai Hospital of Chicago for the ten-year period of 1934 to 1949, inclusive, the war period of 1940 to 1944 being excluded.

The principal pathologic condition encountered was fibroids of the uterus, single or multiple, up to and including the size of a five months' pregnancy. In many instances, adnexal pathology was present and previous laparotomies for pelvic disease had been performed. At our institution, in selected cases, we do not too seriously consider inflammatory diseases of the pelvic organs, size of the tumor, and previous pelvic surgery as a contraindication to vaginal surgery. Our two criteria for surgery from below are that the uterus be moderately mobile and that, in most instances, some degree of relaxation of the vaginal supporting structures be present. Even this latter point is not too strongly stressed, as in nulliparas this operation has been performed with or without previous episiotomy or Schuchardt incision. Campbell, in 1946, stated, "that when a hysterectomy is indicated, the vaginal route is more preferable, and that the bulk of a uterus to be removed is less a contraindication than is the location of its component parts." He remarked further, "Previous pelvic or other abdominal surgery is *not* a contraindication but may complicate both the abdominal or vaginal route." Needless to say, a frozen pelvis or rigid nonmotile uterus should be excluded from vaginal surgery.

Albert Lee, in his report in 1948, violently disagrees with our views as stated above. He states that the only indication for vaginal hysterectomy alone or with associated vaginal surgery, is prolapse of the uterus to at least the second degree. He further states that the largest-sized fibroid to be attempted from below is that of a twelve weeks' pregnancy. Morcellation he particularly condemns, while pelvic inflammatory disease, previous vaginal surgery, poor-risk patients, etc., he considers as definite contraindications.

A comparison with abdominal surgery is not contemplated in this report. Suffice it to say that these 1,121 cases were done while only roughly 700 abdominal operations were performed under the same general routine conditions.

*Presented before the Chicago Gynecological Society, Feb. 16, 1951.

The abdominal series seems large in comparison but we wish to make the point that a greater proportion of abdominal cases was done in the earlier years reported and a great majority of vaginal cases have accumulated in the past five years showing the ever-greater trend to surgery from below. Furthermore, a large number of our abdominal cases were performed even in the second five-year period by the general surgeons.

Contrast these data with those of Kitzmiller in his Grace Hospital Series of 1948. Of 1,689 charts reviewed for the years 1943 through 1947, approximately 82 per cent of his cases were subjected to abdominal subtotal hysterectomy, 9 per cent to total abdominal hysterectomy, and only 0.9 per cent to vaginal hysterectomy. He also gives prolapse as his chief indication. In Campbell's series, 2,798 vaginal hysterectomies were performed as against 898 abdominal uterine extirpations for the like period of time.

Again Rhoades and Zeit of Cleveland in 1946 reported that in 6,017 hysterectomies, 5,732 were done supracervically and only 385 were done vaginally. Large uterine tumor and previous pelvic surgery were their chief contraindications to the vaginal approach.

In our data, which we present, the cases have been divided into those performed for the five-year period of 1934 to 1939, and those for the like five-year period of 1944 to 1949. We have purposely omitted these operations performed for the period of 1939 to 1944 because of the paucity of details on those charts, due to an error in microfilming these case records and the inadvertent omission of many of the important data which we have considered in this thesis.

TABLE I. AGE

AGE (YEARS)	1934-1939		1944-1949	
	NO.	PER CENT	NO.	PER CENT
22	1	0.23		
23	1	0.23		
25	1	0.23		
26	1	0.23	1	0.14
28	1	0.23	1	0.14
30-40	101	23.48	134	18.50
40-50	227	52.79	340	49.10
50-60	74	17.20	147	21.94
60 plus	23	5.32	68	10.14
Total	430	99.94	691	99.96

Table I shows that 430 operations were performed in the first period as against 691 for the second period. The age and percentage of occurrence are as noted; suffice it to say that the largest number of cases falls into the 40- to 50-year-old group and the next largest in the 30- to 40-year-old group, as would be generally expected.

TABLE II. PARITY

PARITY	1934-1939		1944-1949	
	NO.	PER CENT	NO.	PER CENT
Para 0	14	3.72	28	4.05
Para i	27	6.27	88	10.14
Para i plus	389	90.0	575	85.82
Total	430	99.99	691	100.01

Table II gives us the parity of our patients; by far the greatest number, namely 389 in the first group and 575 in the second group having borne more than one child.

TABLE III. PREVIOUS SURGERY

	1934-1939		1944-1949	
	NO.	PER CENT	NO.	PER CENT
Gen. abdominal and gynecological surgery	81	18.83	117	18.95
Abdominal gynecological surgery	29	6.74	60	8.95
Vaginal surgery	17	3.95	23	3.43
Total	127		200	

As to previous surgery, a total of 127 patients in the first group as against 200 patients in the second group had been operated upon prior to their procedures as now performed, the surgery including pelvic surgery. Two hundred patients out of a total of 691 for the second five-year period indicate that nearly one-third of all our vaginal surgery in the past five years has been on patients subjected to previous pelvic surgery, either from above or below.

Contrast this percentage with that of Levinthal, in a paper given recently before this Society, which gives only 6 per cent of his patients operated upon vaginally as having had previous abdominal pelvic surgery. Our survey strongly refutes all previous statements that vaginal hysterectomy is absolutely contraindicated in patients who have had previous pelvic surgery. Two hundred in the second period compared to 127 in the first period show that, after careful study, one may use the pelvic approach for these cases. Waugh, of the Mayo Clinic in 1947 definitely disagreed and placed previous pelvic surgery high up in his list of contraindications to vaginal hysterectomy.

TABLE IV. SYMPTOMS

SYMPTOMS	1934-1939		1944-1949	
	NO.	PER CENT	NO.	PER CENT
Menorrhagia	125	28.37	268	40.00
Prolapse	83	19.30	164	24.47
Metrorrhagia	94	21.86	218	32.59
Urinary symptoms	104	24.18	169	25.22
Abdominal or vaginal pain	137	31.86	205	30.59
Miscellaneous	73	16.97	57	8.50
Vaginal discharge	13	3.02		
No symptoms	3	.69	2	0.29
Tumor of uterus			4	0.59
Therapeutic abortion (fibroids, malignant hypertension, epilepsy)			1	0.44
Postmenopausal bleeding	16	3.72	1	0.44

Symptomatology in gynecological surgery is of course very varied and multiform, many patients having four or five complaints while some have none, the diagnosis being arrived at only by routine physical examinations. The chief symptoms, as shown in Table IV, are of course menometrorrhagia and abdominal pain, two of the most frequent symptoms produced by fibroids of the uterus. Campbell's series contained 1,624 cases of fibroids and 1,138 cases of uncontrolled metrorrhagia. It is interesting to note that prolapse of the uterus, namely, "something dropping out below," was complained of in approximately 20 to 24 per cent of our series, and this symptom is the next most frequently occurring, after menometrorrhagia is disposed of. This high incidence of prolapse occurred in the greatest percentage in the 40- to 50-year group, indicating possibly the great trauma to which the perineum is subjected by childbirth increased in some instances by poor obstetrical care. Contrary to

our teaching of old, prolapse as due to old age was not too evident in our series. Kitzmiller's series corroborates our experience in that prolapse, his chief indication for vaginal hysterectomy, occurred in the highest incidence in the 40- to 50-year group.

TABLE V. CLINICAL DIAGNOSIS

DIAGNOSIS	1934-1939		1944-1949	
	NO.	PER CENT	NO.	PER CENT
Prolapse	106	24.65	233	34.74
Fibroids	117	27.20	390	58.20
Fibrosis	76	17.67	49	7.31
Retroflexion	3	0.69	6	0.89
Hyperplasia	15	3.48	6	0.89
Ovarian cyst	1	0.23	5	0.74
Lacerated cervix	5	1.16	10	1.49
Adenomyosis	2	0.46	16	2.38
Carcinoma of corpus	5	1.46	12	2.44
Carcinoma of cervix	1	0.23	3	0.44
Cervical polyp	6	1.39	10	1.49
Endometrial polyp	1	0.23	6	0.89
Cystocele	1	0.23	3	0.44
Rectocele	1	0.23	4	0.59

Clinical diagnoses presented a varied and difficult picture, and, in many instances, two or more diagnoses were included for the same patient. The principal diagnosis was considered primarily. Table V sets forth that 27 per cent of cases in the first five years and 58 per cent of cases in the second five years were diagnosed primarily as fibroids of the uterus and/or other pelvic pathology, as will be shown when we study the operative procedures performed. The pathological reports give the sizes of these fibroids, and although we have prepared no tables on this fact, a thorough study revealed conclusively that a majority of these fibroids ranged from the size of a twelve weeks' to twenty weeks' pregnancy. Morcellation of the tumor was necessary in approximately 20 per cent of our patients in order to facilitate the operative procedure performed, yet no great difficulties were encountered in the performance of this technique. One of our gynecologists with a large number of vaginal operations personally performed used the conization method of removing the uterus regardless of size and his cases have not been included in this morcellation percentage. This fact bears out Campbell's statement "the bulk of a uterus to be removed is not a contraindication to the vaginal route." He too feels that morcellation is often necessary. The morbidity incident to morcellation is only 11 per cent higher than in nonmorcellation cases.

One interesting feature as brought out in Table V is that carcinoma of the corpus was diagnosed clinically or at least suspected in 1.4 per cent of the cases in the first series and in 2.4 per cent of the cases in the second series. Only one-third of these carcinomas were co-existent with fibroids. These percentages compare very favorably with 1.86 per cent in the first series and 2.08 per cent in the second series proved carcinoma by pathological examination. In these cases a preliminary dilatation and curettage were performed followed either immediately on several days later by a vaginal hysterectomy with bilateral salpingo-oophorectomy. X-ray therapy was finally instituted in most instances. Is this coincidence or are we becoming more expert in our clinical observations or suspicions?

Fibroids of the uterus were by far the most frequently encountered pathological entity. Thirty-eight and eight-tenths per cent in the first series and 55 per cent in the second series showed fibroids in the pathological examination.

TABLE VI. PATHOLOGY

	1934-1939		1944-1949	
	NO.	PER CENT	NO.	PER CENT
Fibroids	167	38.83	369	55.07
Fibrosis	201	46.74	139	20.74
Endometrial hyperplasia	86	20.00	75	11.19
Adenomyosis	39	9.06	108	16.11
Cervical disease	297	69.06	295	44.02
Acute endometritis	5	1.16	3	0.44
Chronic endometritis	22	5.11	37	5.52
Cervical polyp	25	5.81	40	5.94
Carcinoma	8	1.86	14	2.08
Myosarcoma	2	0.46	0	0.0
Gravid uterus	1	0.23	12	1.94
Appendicitis	1	0.23	1	0.14
Associated adnexal disease	22	5.11	37	5.52
X-ray cervicitis	1	0.23	1	0.14
Retained decidual tissue	0		1	0.14
Hyperkeratosis	0		13	1.94

A glance at Table VI gives the varied pathological picture. Here again fibroids were coupled with other pathological entities including adnexal disease, fibrosis, adenomyosis, etc.

Twelve cases in this series were complicated by pregnancy. A thorough study reveals that all twelve were multigravidas between the ages of 39 and 46 years. These uteri contained large multiple fibroids. Five patients presented a bleeding syndrome and in four cases the Aschheim-Zondek test was negative. One pregnant uterus was prolapsed to the second degree in a 42-year-old woman.

Again with reference to Kitzmiller's report, the most common finding in the abdominal hysterectomy group was fibroids of the uterus, and in the vaginal

TABLE VII. SURGERY PERFORMED

	1934-1939		1944-1949	
	NO.	PER CENT	NO.	PER CENT
Vaginal hysterectomy	33	7.67	65	9.70
Vaginal hysterectomy with adnexal removal	6	1.39	29	4.47
Vaginal hysterectomy with posterior plastic	118	27.44	223	33.28
Vaginal hysterectomy with posterior plastic and adnexal removal	11	2.55	47	7.01
Vaginal hysterectomy with anterior plastic	18	4.18	19	2.83
Vaginal hysterectomy with anterior plastic and adnexal removal	2	0.46	7	1.04
Vaginal hysterectomy and anterior and posterior repair	161	37.44	323	48.20
Vaginal hysterectomy and anterior and posterior repair plus adnexal removal	10	2.32	22	3.28
Vaginal hysterectomy and appendectomy	2	0.46	2	0.29
Vaginal hysterectomy and herniorrhaphy	1	0.23	1	0.14
Vaginal hysterectomy and colpectomy	0		1	0.14
Vaginal hysterectomy and hemorrhoidectomy	0		16	2.38

hysterectomy group, fibrosis uteri. Nineteen of his cases showed gravid uteri pathologically. Twelve of these nineteen were associated with fibroids, two were Porro cesareans, and four had no recorded indications. This coincidental gravid condition of the uterus, as we see, thus also occurs in a small percentage of other authors' series of hysterectomies.

Vaginal hysterectomy lends itself to a variegated pattern and allows for a multiplicity of combinations of surgical procedures more or less tailor made to each individual patient's requirements and symptomatology. A study of Table VII will bear out this fact. Certainly, abdominal hysterectomy is more or less routined and not so individually adaptable to each patient's necessities. As related to plastic procedures on the pelvic supporting structures, obviously these patients would require the combined surgical approach for complete cure.

The largest proportion of our patients who had vaginal hysterectomies were subjected also to plastic procedures of one type or another directed both at the anterior as well as the posterior pelvic structures. Herniations with prolapse through either fornix were readily corrected at the same surgical seance. Approximately 71 per cent in the first series and 89 per cent in the second series underwent vaginal hysterectomy with anterior and/or posterior plastic operations combined with some adnexal procedure. Eastman of Vermont in 1948 submitted a report of 1,000 vaginal cases personally performed as against 796 abdominal cases over the same time period. Seven hundred fifty-six of his patients had other pelvic procedures performed along with the vaginal hysterectomy. He states, "On general principles for the patients' best interest, they can be operated upon more favorably through the vaginal approach."

TABLE VIII. MORBIDITY

	1934-1939		1944-1949	
	NO.	PER CENT	NO.	PER CENT
Secondary to surgery	186	43.25	214	31.94
Not attributed to surgery	8	1.86	9	1.34

For an operative procedure to be looked upon with favor, of course the morbidity, mortality, complications, and hospital stay must compare favorably with those of the various other types of surgical procedure recommended to eradicate the condition present. We firmly believe that our last three tables will bear out these facts. As to morbidity, Table VIII shows that 186 cases in the first group, or 43.25 per cent, and 214 cases in the second group, or 31.9 per cent, showed a morbidity which we believe was directly attributable to surgery. By morbidity, we mean a temperature of over 100.4° F. for two consecutive days following the first postoperative day. Kitzmiller had a morbidity "over one day fever" in 34 per cent of his subtotal, 46 per cent of his total, and 64.8 per cent of his vaginal cases. Campbell gives a mean of 64 per cent of his patients subjected to vaginal operations as being nonmorbid. Possibly our lower morbidity rate, and particularly the lower rate in the second group as contrasted to our first group, may be due to present-day freer usage and larger doses of the antibiotics. Only a few of our cases of morbidity were of serious consequence, while the majority cleared up spontaneously. In our morbidity table, we have carefully excluded only 1.8 per cent in the first group and 1.34 per cent in the second group as not attributable to the surgery performed. There were two deaths both in the first five-year period; no deaths in the second five-year period. One death was due to postoperative shock, peritonitis, and ileus with death on the sixth postoperative day; the second death occurred eleven hours postoperatively and was due to hemorrhage.

Complications in our series, always a rather reliable reflection of the quality of the surgery performed, were well within the usual limits for surgery of any type. Table IX indicates that the chief complication and most serious one was that involving the urinary tract.

TABLE IX. COMPLICATIONS

	1934-1939		1944-1949	
	NO.	PER CENT	NO.	PER CENT
Urinary	82	19.30	72	10.74
Vaginal vault infection	45	10.46	58	8.65
Vaginal bleeding	4	0.93	5	0.74
Miscellaneous	37	8.60	35	5.22
Undetermined	32	7.44	49	7.31
Blood transfusion reaction			4	0.59
Pulmonary embolism			1	0.14
Rectovaginal and vesicovaginal fistulas	2	0.11	2	0.28
Pelvic peritonitis	8	1.86	2	0.29
Parotitis			1	0.14

Eighty-two cases, or 19.3 per cent, in the first group and 72, or 10.74 per cent, in the second group suffered urinary complications of one sort or another. By far the largest number of these cases were cystitis and pyelitis up to pyelonephritis. Vesicovaginal and rectovaginal fistulas occurred in two cases in both series, and required subsequent surgery for their correction. In six cases the bladder or rectum was inadvertently opened during surgery but these were sutured primarily at surgery and no fistulas followed. It is interesting to note that the incidence of urinary infection in the second group is much lower than in the first group, namely 10.74 per cent as against 19.3 per cent. Our hospital has been using antibiotic suppositories in the preoperative preparation in most of our vaginal surgical cases. Is this latter fact responsible for our decrease in the number of infectious complications, postoperatively? Vaginal vault infections, usually not a serious complication, occurred as the next most common complication. None of these cases led to serious difficulty and were cleared up rather easily. Only eight in the first group and two in the second group went on to the more serious pelvic infection of pelvic peritonitis. None of these patients died, and the infection merely prolonged the hospital stay and subsequent convalescence.

TABLE X. HOSPITAL DAYS FOLLOWING SURGERY

DAYS	1934-1939	1944-1949
8	5	30
9	18	81
10	61	145
11	55	157
12	54	112
13	39	81
14	35	44
15	18	38
16	12	24
17	6	17
18	6	15
19	4	15
20 plus	15	30

Comparing our complications with those of Kitzmiller, we find that he reports 28 deaths, 10 due to peritonitis and 18 due to noninfection causes. Of

course, his series includes the war years of 1943 to 1945, and his infection incidence may be attributed to the inability to obtain sufficient antibiotics to combat these infections before a fatal outcome became inevitable. Campbell compares a mortality of 1.22 per cent for abdominal cases as against 0.21 per cent for vaginal cases. The mortality in the abdominal operation is thus seen to be six times greater than in the vaginal operation. One final feature of the complications incurred in our series is that only one patient suffered a pulmonary embolism, and this nonfatal. Can abdominal hysterectomy statistics match this feature?

The average hospital stay of the patients included in this report is 12½ days in the first group and 11 in the second group. Table X shows that the largest number of patients were hospitalized from 10 to 14 days. This hospital stay compares favorably with that in Kitzmiller's report of abdominal and vaginal surgery. Ninety-six and eight-tenths per cent of his patients, with both abdominal and vaginal hysterectomies, remained in the hospital 14 days or less, average 12 days.

Comment

In the presentation of these data, the authors have not attempted to renew or carry on the old feud of vaginal versus abdominal hysterectomy. The authors wish only to emphasize that vaginal hysterectomy is a safe procedure for many patients in the hands of experienced vaginal operators. Our operators have been made conscious especially of the vaginal approach to gynecological surgery probably through the indirect influence of Heaney, Kanter, Lash, and others. Because of this influence, our performance of vaginal surgery has become more routine and much less incidental. Gynecological surgery is first thought of from the vaginal approach and then secondarily those cases which might seem to offer serious difficulty from below are relegated to the abdominal approach. From our data presented above, the old indications and contraindications to vaginal surgery would of necessity require revision. When the gynecologists become more conscious of the vaginal operation and more adept at vaginal surgery, the authors believe that the future of vaginal surgery will become brighter and will embrace a broader scope.

Conclusions

1. A series of 1,121 cases of vaginal hysterectomy is herewith presented.
2. Vaginal hysterectomy is the treatment of choice for benign enlargements of the uterus.
3. Previous pelvic surgery and fibroids to the size of a five months' pregnancy are not contraindications to vaginal hysterectomy except in a few instances.
4. Vaginal hysterectomy is easily combined with plastic surgery of the perineum and anterior vaginal compartment, and necessary surgery of existing adnexal pathology.
5. Complications are minimal and morbidity can be held down with antibiotics locally, preoperatively, and postoperatively.
6. Mortality in vaginal hysterectomy is very slight.
7. Hospitalization days are held to a minimum in vaginal hysterectomy.
8. Phlebitis and embolic phenomena are minimal.
9. The authors believe that all gynecologists should be as adept, or even more so, in vaginal as in abdominal surgery.

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Discussion

DR. E. W. FISCHMANN.—This is a worth-while reporting of 1,121 cases of vaginal hysterectomy with a very low mortality and morbidity, and few complications. We can heartily subscribe to the broadened indications that were presented here this evening. We agree with most of the statements and conclusions that were drawn. In regard to the size of the fibroid tumor to be removed, we agree with the authors that size is not a contraindication to the vaginal approach since large tumors can be morcellated and today with the use of Pituitrin or Pitressin and with ample blood for transfusion and antibiotics you can do a morcellation much more safely than it has been done in the past.

In regard to the question of adnexal disease, that, of course, as Campbell has said, may complicate the operation and make removal of the adnexa difficult in certain cases.

In regard to the question of previous operation, that, of course, depends upon the type of operation previously performed. Vaginal operations such as colpoplasty, amputation of the cervix, and even the Manchester operation do not materially complicate a vaginal hysterectomy, but previous intrapelvic operations may offer difficulties because of adhesions of loops of bowel and we feel very definitely that the surgeon who undertakes to do a vaginal hysterectomy on a patient who has had one or two or three previous intrapelvic operations should be well versed in the various techniques of performing the operation of vaginal hysterectomy because in several instances we were compelled to do bisection or hemisection of the uterus in order to liberate the knuckles of bowel that were adherent rather firmly to the cornua of the uterus and could not be visualized accurately and safely enough when the uterus was intact.

In regard to the question of parity, that offers no particular problem. A great many nulliparas can be operated on by the vaginal route. If any difficulty arises we may resort to episiotomy or the Schuchardt incision.

In regard to some of the questions about this report, we wonder if the enthusiasm of the authors to do vaginal hysterectomies in a large percentage of their cases did not lead them to unnecessary sacrifice of uteri in young women, as was presented in Table I. There were seven or eight women under 30 years of age who lost their uteri because of vaginal hysterectomy. There were several in the second group, the 30-to-40 age group. We firmly believe that a woman has a right to keep her uterus and we should try to conserve it. We feel that perhaps in some of these cases, if an abdominal operation had been done, conservative myomectomy might have saved the uterus for some of these women.

In regard to the question of carcinoma, we believe that vaginal hysterectomy is not the operation of choice for cases of carcinoma, either corporal or cervical, for the simple reason that there is danger of contamination, and, second, we are not always certain that we can remove the adnexa which is of paramount importance in cases of hysterectomy for carcinoma. Then, too, we want to point out that the authors had a rather small percentage of adnexal removals in these cases when we consider the large group of patients who were over 40 years of age. The authors did not mention anesthesia. The vaginal route is the operation of choice in the bad-risk patient who needs a hysterectomy, and it can frequently be performed under local anesthesia.

DR. AARON E. KANTER.—Once again an essayist has brought to the attention of the Society the feasibility and safety of the vaginal approach for pelvic surgery. Although the majority of the operations reported were performed by qualified and experienced gynecologists, there were a number of patients included in this group who were cared for by the resident staff and by general surgeons with no specialized gynecologic training. In spite of this, the results approximate those found in other series reported and published.

The incidence of carcinoma (1.04 per cent in the first group and 2.08 per cent in the second group) was quite high, and the question arises as to whether these patients had had preliminary radiation therapy before surgery. I know that many of them did not have this, because they were operated upon before we began to follow this procedure. I also wonder how many of the patients who had the uteri removed by morcellation had corpus malignancy. We now feel that before a vaginal hysterectomy by morcellation, a dilatation and curettage should be done to rule out malignancy. If this complication is found to be present, radiation therapy should be instituted and completed before the surgery is attempted.

This series shows a rather high incidence of pregnancy in the uteri removed. I do not know how many of these patients had a diagnosis of pregnancy made before surgery, but I do believe that such a diagnosis can be made in most instances without resorting to the Friedman test. An accurate history and a good pelvic examination should establish a diagnosis in spite of a negative biologic test. This report does emphasize the fact that when a uterus is to be removed vaginally for benign pathology, the addition of an early pregnancy is no contraindication to the employment of the vaginal approach.

The morbidities of 43.5 per cent and 31.9 per cent, with 101° F. used as the criterion, are high. These have now been materially reduced by the preoperative use of the penicillin suppository and by proper preparation of the patient. By this is meant cleaning up foci of infection, building up proper nutrition, reducing weight in obese women, and cleaning up local pathology such as vaginitis and cervical infection. Had this been done in this series there would not have been 10 cases of pelvic peritonitis. The incidence of general peritonitis was high, but fortunately no deaths resulted. It would be of interest to know if these complications were more common in the group of morcellations.

The startlingly low incidence, or almost complete absence of embolic phenomena is a great argument in favor of the vaginal operation.

Once again we have demonstrated that the vaginal approach for hysterectomy can be employed in spite of a history of previous pelvic surgery and nulliparity. When the surgeon uses the same degree of caution in vaginal surgery that he uses in opening the abdomen in a patient with previous abdominal incisions, accidental damage can be kept to a minimum. I grant that the vaginal route should not be followed where subacute inflammatory process or extensive endometriosis are present. Nor do I believe that a vaginal hysterectomy should follow a dilatation and curettage by two days. This sequence of events should ensue immediately or a period of one week should elapse before the more major operation is performed.

It is my opinion that series of cases such as this, and those previously reported before this group should convince the skeptic that it is feasible to do a major portion of gynecological surgery by the vaginal approach. Any uterus that can be moved from side to side and that can be made to descend slightly by downward traction in a pelvis, that is not fixed by inflammation or endometriosis, can be removed vaginally.

DR. ARTHUR H. KLAWANS.—I believe that probably the incidence of carcinoma in patients who have vaginal hysterectomy will increase when we recognize carcinoma in situ as an indication for vaginal hysterectomy. The incidence of urinary-tract infections will decrease if we follow the routine, as in some institutions, where antibiotic or chemotherapeutic therapy is used whenever and as long as an indwelling catheter is in place.

DR. GOLDEN (Closing).—In answer to Dr. Fischmann, as to the ability to do a vaginal hysterectomy in cases of previous pelvic surgery, I might add that in many cases we had some difficulty in doing the same operation abdominally as vaginally. It is true that the dissection must be done a little more carefully but it is feasible and possible.

In answer to the question concerning vaginal hysterectomy in our women in the young age bracket; these women were all multiparous women and all had fibroids with symptoms.

For carcinoma of the body of the uterus done vaginally, there is a difference of opinion but the operators at the hospital feel that, where there is no extension, the operation can well be done vaginally and that with vaginal hysterectomy the adnexa can very easily and rapidly be removed. We did many of these operations under pudendal block together with slight Novocain infiltration into the upper portion of the broad ligament, and spinal anesthesia.

In answer to Dr. Klawans' statement, we do not have any statistics on the question of carcinoma treated by morcellation.

In regard to the pregnant patients submitted to vaginal hysterectomy, in the 12 presented we had five with menometrorrhagia, four had negative Aschheim-Zondek tests, one had a prolapse, and two were for therapeutic abortions, one because of an anginal syndrome and the second because of malignant hypertension with epilepsy.

In answer to Dr. Allen, we do not have any follow-up on our cases of carcinoma of the body of the uteus. We certainly agree with Dr. Allen that dilatation and curettage should precede all vaginal hysterectomies.

I should like to preface our general remarks by agreeing with Dr. Allen who, in 1950, stated, "Vaginal hysterectomy should be the method of removal whenever possible and in skilled hands it is safer for the patient than abdominal hysterectomy and does not cause as much discomfort." We like to believe that when the indication for hysterectomy is present our first consideration is to do the operation vaginally rather than abdominally unless a specific contraindication, as herewith presented, exists. Dr. Heaney, in his discussion on vaginal hysterectomy in 1949, aptly states, "It is interesting to note that those who persist in perfecting themselves in the technic of vaginal hysterectomy gradually disregard more and more of the contraindications so insistently laid down by those with little or no familiarity with the operation." As the number of vaginal hysterectomies in our hospital increases skill of the operators concerned warrants their increased "daring," as some would call it, in doing the more complicated forms of vaginal hysterectomy. We believe that prolapse of the uterus should not be the number one indication for vaginal hysterectomy.

It has been our practice not to use irradiation therapy for the benign uterine enlargements. Dr. Allen, as late as 1950, relates that, "It is our firm conviction that irradiation should not, except in the most exceptional cases, be used for benign diseases in the female pelvis. Most certainly it should never be used in the ordinary doses used for castration until the absence of carcinoma has been confirmed." He further emphasizes that fibroids larger than two fists should not be irradiated. Dr. Heaney states that he has never yet substituted radium therapy in a patient in whom vaginal hysterectomy was indicated.

When surgery is necessary in the aged and in patients with systemic medical disabilities vaginal hysterectomy is the safer procedure. Heaney is of the opinion that under comparable conditions shock is extremely rare, anesthesia is shorter, ileus seldom occurs, and the patient has a smoother and shorter convalescence.

Drs. Edwards and Beebe in their series of 570 vaginal hysterectomies removed 36 uteri in which the fibroids ranged in size to that of a three to four months' pregnancy. Benign tumors extending above the umbilicus have been removed vaginally following morcellation.

Inspection of the adnexa is a routine procedure by the gynecologists represented in our series; and adnexal pathology is then adequately dealt with through the vaginal approach.

We believe that there are few definite contraindications to vaginal hysterectomy although there are certainly instances in which the transabdominal approach is preferable.

PREGNANCY COMPLICATED BY SUBARACHNOID HEMORRHAGE

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SINCE Wilks'[1] brief account of the postmortem findings of a case of subarachnoid hemorrhage in 1859, and Bramwell's[2] paper in 1896, subarachnoid hemorrhage has been established as a relatively common clinical entity. The medical literature is replete with reports of large numbers of such cases. However, subarachnoid hemorrhage (hereafter referred to in this paper as SAH) is a rare complication of pregnancy. Although Gerin-Rose[3] reported the first case in 1859, a review of the world's literature to date reveals only 29 cases of SAH complicating pregnancy. Moskowitz and Schneider[4] in 1938 found 13 cases reported up to that date, in addition to reporting their own 3 cases. Garber and Maier[5] in 1948 presented 3 of their own cases and mentioned 4 other cases occurring in the literature. A review of the individual reports reveals that many of them are fragmentary and incomplete. The interrelationship of SAH and pregnancy has not been clearly demonstrated from the papers reviewed. The purpose of this paper is to report 3 additional cases of SAH in pregnancy seen by the author and to compile those cases reported to date, in an attempt to evolve a clear picture of the relationship between SAH and pregnancy.[6-12]

Case Reports

CASE 1.—A. L. O., a 24-year-old primipara, was admitted to the hospital on Aug. 15, 1946, at 2:30 P.M., in coma. The history revealed that she was 6½ months pregnant and had been under prenatal care by a physician. The antepartum course was uneventful. When seen at home by a physician, she was unconscious on the floor. The pupils were dilated, equal in size, and reacted sluggishly to light and accommodation. She had frequent repeated tonic convulsions with spasms of both upper extremities. The lower limbs were held in rigid extension. The head and neck were hyperextended. Opisthotonus was present. The blood pressure at this time was 140/100. On admission to the hospital, the blood pressure was 90/50. The pulse rate was 92. The size of the uterus was that of a 6½ months' gestation. The fetal heartbeat was present, regular, and the rate 132. Moist râles were present in the lungs bilaterally. Examination of the heart revealed no remarkable changes. There was no edema of the extremities present. There were hyperactive knee jerks and ankle jerks. Laboratory findings at the time of admission revealed the following: Blood sugar 202 mg. per cent, blood urea nitrogen 13 mg. per cent, carbon dioxide combining power 22 vol. per cent. Urine revealed 3+ sugar, 3+ albumin, and 4+ acetone.

At this time it was believed that the patient was in a diabetic coma and 1,000 c.c. of 10 per cent glucose in saline were started. The patient was given 50 units of insulin. However, her condition deteriorated rapidly and she ceased to breathe at 4:45 P.M. Cesarean section was immediately performed with delivery of a living child. No respirations were noted, but the heart was beating at the rate of 25 per minute. The baby died at 5:30 P.M.

Autopsy Findings.—The significant findings at autopsy were that the aorta appeared thinner than usual, with a decrease in its elasticity. The arteries in general showed a hypoplasia with loss in elasticity. On removal of the calvarium it was noted that there was a marked subarachnoid hemorrhage present over the entire cortical surface of the brain. The arteries of the Circle of Willis and the vertebral arteries appeared hypoplastic, thin, and almost membranous in some areas. Careful dissection of the brain revealed no definite bleeding points.

Final Diagnosis.—Subarachnoid hemorrhage.

CASE 2.—A. R., 33 years old, a white primipara, was admitted to the hospital in stupor on Aug. 21, 1947, at 9:35 A.M. Past history obtained from the husband revealed that the patient's expected date of confinement was Dec. 22, 1947. The patient was under the care of a private physician and the pregnancy was uneventful until 2 months prior to admission when she began to complain of swelling of the legs and headaches. The headaches had been very severe for the past two weeks and were associated with nausea but no vomiting. On the day of admission, the patient awoke at 2 A.M., complaining of nausea, weakness, and severe headache. She then fell asleep until 5 A.M., at which time it was noted she had difficulty in speaking and was very weak. She lapsed into a semistuporous condition and was brought to the hospital. Physical examination on admission revealed an acutely ill woman lying quietly in bed. She could not be roused, but reacted to external stimulation. The pupils were round, regular, equal in size, and reacted to light and accommodation. There was noted at this time a questionable drooping of the right angle of the mouth. The blood pressure was 168/104. Respirations were 100. The chest was clear to percussion and auscultation. Examination of the heart revealed no murmurs and the sounds were good. On palpation of the abdomen, it was noted that the uterus was enlarged to 3 fingerbreadths below the xiphoid. The fetal heartbeat was heard in the right lower quadrant; rate was 144, regular. There was a marked 3 plus pitting edema of the legs, extending to the thighs. There were hyperactive knee, ankle, and elbow jerks. The Babinski reflex was questionable and there was no nuchal rigidity. There were absent abdominal reflexes. The left arm was flaccid. The urine, on admission, revealed a 4 plus albumin, specific gravity 1.022, with many casts and white blood cells. The patient was immediately started on dehydration therapy and sedation consisting of intravenous administration of 50 c.c. of 50 per cent glucose, and 20 c.c. of 10 per cent magnesium sulfate, oxygen, and morphine sulfate. As her condition did not improve despite all therapy, it was conjectured that perhaps she had a subarachnoid hemorrhage superimposed on a severe toxemia of pregnancy. A diagnostic spinal tap was performed at 8 P.M. of the same evening. All the tubes contained frank blood. The dynamics were as follows: The initial spinal fluid pressure was 270 mm. of water. Queckenstedt reaction on the right was 400 mm. of water, on the left 500 mm. of water. After removal of some spinal fluid, the pressure was 132 mm. of water. Blood chemistry revealed a carbon dioxide combining power of 40 mg. per cent, sugar 115 mg. per cent, urea nitrogen 15 mg. per cent. At 10:45 of the same evening, while receiving 30 c.c. of 10 per cent magnesium sulfate intravenously, the patient suddenly stopped breathing and became cyanotic. Artificial respiration was immediately instituted, and intravenous Coramine was administered. She responded immediately and began breathing. The neurological consultant suggested that spinal taps be repeated every 12 hours to alleviate the increased intracranial pressure. An eye consultant that same evening found slight papilledema of the discs. The nasal margins were rather blurred and there was an elevation of the discs of approximately 1 diopter. The retinal vessels were rather tortuous, but the arteries were of normal caliber. The veins were rather engorged. No hemorrhages or exudate were noted. Spinal tap at 10:30 the next morning revealed a grossly bloody fluid. The initial pressure was 280 mm. water. Final pressure was 170 mm. water. The pulse rate was 140, the blood pressure 140/110. Despite all therapy, the patient's condition became progressively worse, the coma deepened, and she developed pulmonary edema. The temperature became progressively higher until just prior to death when the rectal temperature reached 108° F.

Permission for autopsy was not obtained.

Final Diagnosis.—Subarachnoid hemorrhage superimposed on toxemia of pregnancy.

CASE 3.—P. G., a 23-year-old white woman, 8 months pregnant, was admitted to the hospital on July 29, 1948, at 3 P.M. On admission, it was noted that the patient was markedly cyanotic, dyspneic, and unable to answer questions. History obtained from a cousin revealed that the onset of the symptoms began following a coughing spell which occurred while the patient was eating. The initial impression at this time was that she had a foreign body in the respiratory tract. History obtained from the husband revealed that she had been coughing for the past week. Her last menstrual period was Nov. 5, 1947; the expected date of confinement was Aug. 12, 1948. The present pregnancy had been uneventful except for a cold during the past month. Physical examination on admission revealed a well-developed, well-nourished woman in coma, with marked cyanosis of the face, fingers, and nailbeds. Blood pressure was 120/70, pulse rate 130, temperature 101.2° F. The pupils were miotic and fixed to light. The neck was rigid. Coarse rhonchi were heard throughout both lung fields. The uterus was enlarged to 2 fingerbreadths above the umbilicus. The fetal heart tones were heard in the right lower quadrant, 148 per minute. No petechiae or edema were noted. Under direct laryngoscopy, no foreign bodies were noted in the larynx. The vocal cords appeared normal and freely movable. Bronchoscopy revealed no foreign body present in the tracheobronchial tree. The vomiting and gag reflexes were absent. An intratracheal catheter was introduced and the patient was given oxygen by catheter. With the introduction of the intratracheal catheter, the patient began bringing up a brownish fluid and began foaming at the mouth. At this time, she became markedly cyanotic. She ceased to breathe at 8:45 P.M. Immediate postmortem cesarean section was performed with delivery of a girl infant. Although fetal heart sounds were present at birth, they ceased after 35 minutes. At no time did the baby breathe spontaneously. It is to be noted that immediately prior to the performance of the cesarean section, the fetal heart tones were heard indistinctly. A postmortem spinal tap revealed bloody fluid in all tubes. The blood did not clot. The initial spinal fluid pressure was 380 mm. water.

X-rays of the chest just prior to death were negative. The urine was negative for albumin and revealed a 2 plus glycosuria.

Postmortem findings revealed a marked injection of the blood vessels of the dura. There was flattening of convolutions of the brain. At the base of the brain, there was noted a marked subarachnoid hemorrhage in the region of the Circle of Willis, which extended over the inferior surface of the pons and cerebellum. There was a rupture of an aneurysm of the posterior branch of the cerebral artery on the left side. The blood vessels of the Circle of Willis were thin walled and appeared sacculated in a number of areas. Section of the brain showed no hemorrhage intracerebrally; there was a moderate hypertrophy of the pituitary gland.

Final Diagnosis.—Spontaneous subarachnoid hemorrhage, secondary to rupture of an aneurysm of the Circle of Willis.

Pathogenesis

Subarachnoid hemorrhage, characterized by bleeding into the subarachnoid space, may be either spontaneous or secondary. Primary or spontaneous subarachnoid hemorrhage results from rupture of a subarachnoid vessel. In the series of Helpern and Rabson[13] and others, the major source of bleeding was the rupture of a saccular aneurysm of one of the cerebral arteries. In a great many cases, however, the source of rupture is not found at the autopsy table. The theories as to the mechanism underlying the formation of the vessel wall defect differ among the various authorities. Forbus[14] is of the opinion that the lesions are acquired and are dependent on a congenital defect in the muscularis at the points of bifurcation, and the subsequent degeneration of the internal elastica

due to continued overstretching by the force of the blood pressure. Carmichael[15] observed defects in the elastic tissue concentrated in the internal elastic membrane as well as in the muscularis and was of the opinion that a defect in one could be resisted by the adequacy of the other. However, based on embryologic studies, Bremer[16] concludes that aneurysms are actually congenital in their development and are already existent in the embryo and at birth.

The bleeding may be confined to focal brain areas or may be widespread over the entire brain. The hemorrhage may vary from a few to many millimeters in thickness.

Subarachnoid hemorrhages have been attributed to "trauma, arteriosclerosis, septic or infectious emboli, ruptured intracranial aneurysms, massive cerebral hemorrhage invading the subarachnoid space, intraventricular hemorrhage, blood dyscrasias, ruptured vascular neoplasms, lues, cardiorenal disease, tuberculosis, hemophilia, leukemia, Hodgkin's disease, pernicious anemia, measles, diphtheria, diabetes, epilepsy, pertussis, sepsis and subacute bacterial endocarditis" (Alpers[17]).

The hypertension of pre-eclampsia and the convulsive efforts of marked eclampsia are also precipitating factors in causing subarachnoid hemorrhage. Eller[18] reported that 15 per cent of the autopsies on eclamptics showed evidence of gross hemorrhage in contrast to the infrequency of the diagnosis. DeLee[19] found cerebral hemorrhage in 40 per cent of autopsied eclamptics. In Parks and Pearson's[20] series of 41 eclamptics, 4 patients died. All 4 showed gross evidence of subarachnoid hemorrhage.

Of the cases reviewed, 12 patients showed evidence of toxemia of pregnancy manifested by edema, albuminuria, and hypertension prior to the onset of symptoms of subarachnoid hemorrhage.

Incidence

Subarachnoid hemorrhage is a disease of middle age, rarely seen under 20, and most commonly found between the ages 20 and 59 years. Seventy-four per cent of Magee's[21] cases occurred between the ages of 21 and 40. In Helpern's and Rabson's[13] series, 84 per cent of the cases occurred between the ages of 20 and 59.

TABLE I. AGE DISTRIBUTION OF SAH COMPLICATING PREGNANCY

AGE (YEARS)	NO. OF CASES	PERCENTAGE
10-19	1	4
20-29	14	56
30-39	8	32
40-49	2	8

Although the number of cases is not great enough to be statistically significant, it is interesting to note that the majority occurred between ages 20 and 39 years, the period of greatest fertility. Parity seems to play no significant part since 12 cases occurred in primiparas and 10 cases occurred in multiparas. No cases occurred in the first two trimesters of pregnancy. Eleven cases occurred in the third trimester.

The circumstances immediately preceding the onset of symptoms reveal that active labor was followed by the onset of symptoms of SAH in 13 cases. Four of these patients received oxytocics at some time during the third stage. In 15 cases, the symptoms of SAH were not preceded by active labor. In only one case did symptoms begin while the patient was in active labor.

In 8 cases, symptoms of SAH appeared within 12 hours following labor and delivery. Within 24 hours, 3 additional cases of SAH were noted. When SAH

occurred following labor, 8 of the patients died and 5 recovered. Of the 15 cases that occurred without labor, 10 of the patients died and 5 recovered. Of the five patients who recovered, 2 had cesarean sections performed.

The relationship of labor and delivery to SAH is a coincidental one, inasmuch as active labor did not cause an increase in the number of cases of SAH, nor did it increase the mortality of the patients with SAH.

Symptoms

The symptoms of SAH are protean, varying with the amount of blood escaping into the subarachnoid space at the time of hemorrhage.

A. Slow Leaks.—The symptoms may be intermittent in character.

1. Periodic increases in intracranial pressure may result in recurring headaches resembling migraine.

2. Deposition of fibrin around the medulla and upper portions of the cord may cause pain and stiffness in the neck.

3. If the leakage of blood persists, with an increase in intracranial pressure, there may be vomiting, cervical rigidity, headaches, and temperature rises.

B. Sudden Rupture.—This results in a dramatic apoplectic onset of symptoms, i.e., headaches, convulsions. They may be accompanied by vomiting and are often followed by unconsciousness and death. Occasionally prodromas may be present in the form of mild headaches, tinnitus, and giddiness. The headaches are severe, sudden in onset, and may be frontal, temporal, or occipital in location. The pain often radiates to the back of the neck.

In 13 cases, the onset of an attack of SAH was characterized by headache. Vomiting was the initial symptom and accompanied headaches in 6 cases. In 8 cases, the patients had complained of headache prior to the onset of the present attack and 3 of these cases had been diagnosed as migraine. Of these 13 patients, 8 died and 5 recovered (Table II).

TABLE II. SYMPTOMATOLOGY AND MORTALITY OF SAH IN PREGNANCY

SYMPTOM	INITIAL	DIED	RECOVERED	ACCOMPANYING	DIED	RECOVERED
Headache	13	8	5			
Vomiting	6		6	1		1
Unconsciousness	5	5	0	17	15	2
Convulsions	3	2	1	2	1	1
Loss of vision	2	1	1			
Cyanosis	2	2	0	2	2	
Mental confusion	2	1	1			
Vaginal bleeding	2	1	1			
Aching in back of legs	1		1	1		1

Unconsciousness may be apoplectic in onset or may follow, at any time, the initial symptoms. The degree of unconsciousness may be mild or severe. Sudden onset of unconsciousness characterized the explosive onset of SAH in 4 cases. All 4 patients died, an indication of the gravity of the condition when unconsciousness is the initial symptom. In 17 cases, unconsciousness was an accompanying symptom. Of these patients, 15 died and 2 recovered.

Mental derangements are not uncommon. They may be fleeting or may persist for weeks or months. "The picture may resemble that of a confusional psychosis with clouding of the sensorium and marked delirium" (Alpers[17]). The attack was initiated with mental confusion in 2 cases. One of these patients died and one recovered. Atypical eclamptic convulsions were noted in three cases. Two of these patients died and one recovered. Convulsions were an accompanying symptom in two cases.

Neurological signs are noted quite often. One of the most outstanding signs is that of meningeal irritation manifested by stiffness of the neck with positive Babinski and Kernig signs. These signs may or may not be present even with marked bleeding. They may be fleeting and disappear even before complete recovery, or they may persist for a long time. With hemorrhage at the base of the brain and bleeding into the optic sheath, cranial nerve palsies and papilledema of various degrees are noted. As a group, these cases are not favorable for surgical treatment. Two cases were inaugurated with loss of vision; one patient died and one recovered. With hemorrhage into the acoustic sheath, deafness, tinnitus, and vertigo are present. One case began with deafness. Facial palsies follow hemorrhage into the facial nerve sheath. With seepage of blood into the spinal subarachnoid space, pain in one or both legs may be present. The one patient whose initial symptom was aching in the back and legs recovered. SAH was initiated with vaginal bleeding in two cases. Of these patients, one died and one recovered. Cyanosis initiated the attack in two cases and both of these patients died. It was noted as an accompanying symptom in two cases.

The deeply blood-stained cerebrospinal fluid is characteristic of this disease. The cells may be centrifuged to the bottom of the tube or will settle down, leaving a supernatant fluid that is clear or tinged by hemoglobin. One week after the attack, the supernatant fluid is xanthochromic. Only the white blood cells are apparent since they are not as readily destroyed as the red cells. The pressure of the spinal fluid may be normal or elevated. Of the cases in which spinal taps were performed, 20 had bloody spinal fluids and two had turbid fluids.

At the time of the onset of symptoms, 14 patients had varying amounts of albuminuria and four had no albuminuria. In three cases, there was no albuminuria present just prior to the attack, but with the onset of the attack, marked degrees of albuminuria were present. This phenomenon was first noted by Widal[22] in 1903 when he commented on the transient massive albuminuria that accompanied subarachnoid hemorrhage. He believed the etiological factor to be pressure of the hemorrhage on the brain stem. Schneider[23] reported 5 cases of albuminuria and subarachnoid hemorrhage from the literature. He stressed the large quantity of albumin and the absence of free blood in the urine occurring during or immediately following SAH, with a tendency to rapid diminution of the albuminuria. Symonds[24] feels that "albuminuria is a rare accompaniment of SAH although there is good physiological evidence for supposing that this albuminuria may be due to a disturbance of the nerve centers concerned with renal secretion. At present, proof is lacking that the symptoms may occur simply as a result of SAH in persons with healthy kidneys."

Hypertension was reported in 13 cases at the onset of symptoms. The blood pressure was normal or below normal in eight cases and not recorded in the remaining instances. The blood pressure is of no significance since the increased intracranial pressure may cause the blood pressure to rise or cause an elevated pressure to fall when shock supervenes.

Diagnosis

The apoplectic onset of headache and coma in a relatively young woman with or without hypertension, associated with a grossly bloody spinal fluid, is pathognomonic of subarachnoid hemorrhage. More often than not, a pregnant woman with the above symptoms first has a diagnosis of toxemia of pregnancy, until further work-up or the findings at the autopsy table show the correct diagnosis. Although hypertension, albuminuria, headaches, convulsions, and

coma are common to both conditions, grossly bloody spinal fluid does not occur in eclamptic toxemia no matter how severe the toxemia. As a rule, sedation and dehydration will help clear up all but the most severe of toxemias. This regime will have only a minimal effect on subarachnoid hemorrhage.

SAH is differentiated from meningitis by the absence of a septic temperature and the absence of a pathogenic microorganism in the spinal fluid. While the presence of blood in the spinal fluid is not unknown in meningitis, its frequency is not as great as in SAH.

Epidemic encephalitis is differentiated from SAH in that it is rarely accompanied by hemorrhage.

Subdural hemorrhage may exist with SAH. The spinal fluid in subdural hemorrhage is not bloody, but with rupture into the arachnoid space, the spinal fluid resembles that of a primary subarachnoid hemorrhage.

Inasmuch as SAH and brain tumor may both be accompanied by prodromas, headaches and choked discs, the absence of a bloody spinal fluid points to the correct diagnosis of a brain tumor.

The age of the patient will usually suffice to differentiate the cases of cerebrovascular accidents from those of SAH since cerebrovascular accidents tend to occur in the older age group.

Urinary findings of albuminuria and/or glycosuria might lead to a false diagnosis of either uremia or glycosuria unless the clinician is aware of the possibility of subarachnoid hemorrhage causing these symptoms. Further urinary work-up and blood chemistry findings will aid in the proper diagnosis.

Prognosis

SAH is the cause of sudden death in from 2 to 4.5 per cent of all cases. In Wolf's[25] series, 29 per cent of the patients died during the first episode and 14 per cent died with recurrent bleeding in from two to four weeks. In different series, the mortality varied from 28 to 50 per cent. In those who survived the first episode of bleeding, the threat of recurrent hemorrhage is ever present, since bleeding tends to recur in approximately 35 per cent of the cases.

The period of recurrence may vary from days to years, with death usually occurring with subsequent attacks. In the cases reviewed, 18 of the patients died and 10 recovered.

TABLE III. AGE AND MORTALITY OF PREGNANT WOMEN WITH SAH

AGE (YEARS)	DIED	RECOVERED
10-19	1	
20-29	10	6
30-39	5	3
40-49	2	1

Unconsciousness is of great prognostic significance inasmuch as 100 per cent of the patients died when it occurred as the initial symptom of SAH. Eighty-six per cent of the patients died when unconsciousness supervened.

Subarachnoid hemorrhage, superimposed on eclampsia, is of very grave prognostic import. Eleven, or 81 per cent, of these patients died. Only 2, or 19 per cent, of the eclamptics with superimposed SAH recovered. In Parks and Pearson's[20] series of 41 eclamptics, all 4 eclamptics who died showed gross evidence of subarachnoid hemorrhage. In Eller's[18] series, 15 per cent of the autopsied eclamptics showed gross hemorrhage. DeLee[19] states that 40 per cent of all autopsied eclamptics showed evidence of cerebral hemorrhage.

Treatment

Although utilized primarily for establishing a diagnosis, spinal tap is to be used as a therapeutic measure only when signs and symptoms point to progressive increasing intracranial pressure. In the presence of active bleeding, spinal tap is not to be performed since the decrease of the intracranial pressure will lead to further bleeding. Masten[26] recommends lumbar puncture for establishing a diagnosis and cisternal puncture for reducing the progressive intracranial pressure. In any event, the spinal fluid should be removed slowly, and not more than 15 to 20 c.c. are to be removed at any one time.

When the bleeding has ceased, and if the patient remains in coma or if there are signs of increased meningeal irritation, spinal tap is to be performed to relieve the increased intracranial pressure and to remove the irritating products of hemorrhage. Sedation and bed rest are advised, and undue excitement on the part of the patient is to be avoided at all costs. Hypertonic solutions of glucose in concentrations of either 25 or 50 per cent are to be administered intravenously to aid in the hydration of the patient, to maintain a caloric balance, and to provide nourishment. Magnesium sulfate administered intramuscularly helps to reduce intracranial pressure, and quiet the patient. Convalescence is to be prolonged and the patient is permitted to resume physical activity slowly and gradually. If the patient survives the attack, but has continued symptoms, arteriograhpy can be performed in an attempt to localize the lesion. If it is possible to localize the lesion, surgical intervention is to be attempted whenever feasible. Prior to surgical intervention, the over-all mortality due to rupture of an aneurysm was 100 per cent, but with surgical intervention the mortality has now been reduced to 25 to 36 per cent (Dandy[27]).

SAH is no contraindication to the continuance of pregnancy. Cesarean section is not indicated in these cases other than for obstetrical reasons, inasmuch as there is no increase in mortality when the patient has undergone the rigors of active labor.

Summary

1. Twenty-nine cases of subarachnoid hemorrhage complicating pregnancy are reviewed from the world's literature.

2. Three new cases of SAH in pregnancy that occurred in the author's experience are presented.

3. SAH is a rare and formidable complication of pregnancy. Injection of oxytocics might be precipitating factors in causing rupture of silent cerebral aneurysms of pregnant women. Oxytocics should be administered with extreme caution to those women who have complaints of recurrent headaches or migraine.

4. Unconsciousness due to SAH is of grave prognostic import, since a very large percentage of these patients die.

5. Cesarean section in a pregnant woman with SAH is to be performed only for obstetrical indications, as the absence of labor prior to an attack does not significantly reduce the mortality.

6. Pregnancy does not alter the clinical picture of subarachnoid hemorrhage.

7. It is incumbent upon the physician to perform an adequate neurological examination and spinal tap on all unconscious pregnant women in order to make the correct diagnosis and institute proper treatment at the most feasible

time. Failure to do so will result in overlooking the presence of a subarachnoid hemorrhage, which will be found more often than a review of the literature indicates.

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134 HEMPSTEAD AVENUE

ABORTIONS—A STUDY BASED ON 1,304 CASES*

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The problem of abortions is a major one at Charity Hospital in New Orleans. This institution receives the greater portion of abortion cases occurring in the indigent of New Orleans. The types of complications in such cases are manifold, because this hospital receives the most serious cases from the entire state of Louisiana. Since there have been no recent surveys of this problem on the Tulane Service at this institution, this study was undertaken.

Material

During the 54-month period ending June 30, 1950, 1,304 patients with abortions were admitted on the Tulane Gynecologic Service at Charity Hospital of Louisiana in New Orleans. These cases comprise abortions of all types during the first two trimesters of pregnancy but do not include patients treated in the outpatient clinic. Of the entire series 447 patients (34.3 per cent) were white and 857 (65.7 per cent) Negro, a ratio of about 2:1, which is about the same as for all gynecologic admissions. The types of abortion according to color of the patient are shown in Table I. The diagnosis on admission for the spontaneous group is shown in Table II. The initiating factor in the patients not definitely known to have had criminal interference was not recorded, or the history was too vague in the majority of instances to be reliable.

TABLE I. TYPES ACCORDING TO COLOR IN 1,304 ABORTIONS ON THE TULANE SERVICE, CHARITY HOSPITAL, FROM JANUARY, 1946 TO JULY, 1950

TYPE	NEGRO	WHITE	TOTAL
Spontaneous	794	377	1,171
Criminal	42	61	103
Suspected criminal	14	8	22
Therapeutic	7	1	8
Total	857	447	1,304

TABLE II. DIAGNOSIS ON ADMISSION IN 1,171 SPONTANEOUS ABORTIONS, TULANE SERVICE, CHARITY HOSPITAL, FROM JANUARY, 1946 TO JULY, 1950

	NEGRO	WHITE	TOTAL
Threatened	107	54	161
Incomplete	489	255	744
Complete	193	66	259
Missed	5	2	7
Total	794	377	1,171

*Read before the meeting of the New Orleans Obstetric and Gynecologic Society, Oct. 30, 1950, in New Orleans.

Incidence of Occurrence

The incidence of occurrence for the years comprising the study revealed a slight increase for Negroes but a relatively constant rate for white women, with the exception of the year 1948, which showed a significant but unexplainable drop (Fig. 1). That this may have been true for the state of Louisiana will be shown later (Fig. 13). Fig. 2 compares the number of admissions of abortions for each year at Charity Hospital with that for a private hospital, and Fig. 3 compares the number of term deliveries on the Tulane Service for the respective years with that for the private hospital. As can be seen, there has been a slight but definite decrease in the number of private deliveries, with a comparable increase of the deliveries at Charity Hospital but no significant change in the abortion rate.

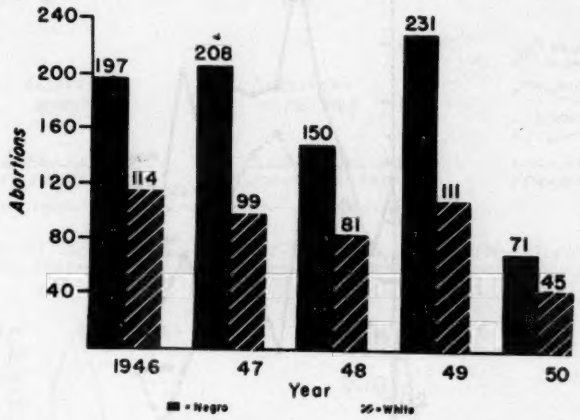

Fig. 1.—Number of abortions in white and Negro patients on Tulane Service, Charity Hospital in New Orleans, from January, 1946, to July, 1950.

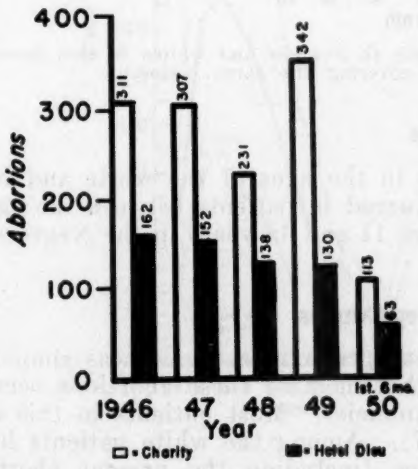

Fig. 2.

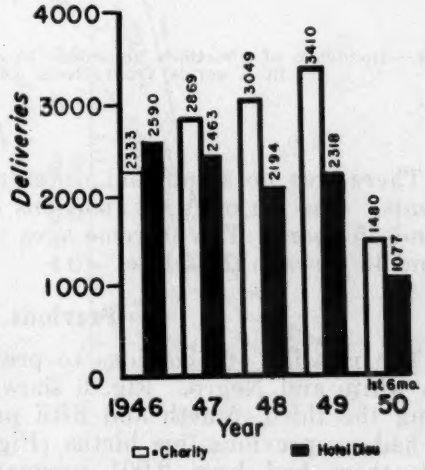

Fig. 3.

Fig. 2.—Comparison by year of abortions on Tulane Service, Charity Hospital in New Orleans, and Hotel Dieu from January, 1946, to July, 1950.

Fig. 3.—Comparison of deliveries by year on Tulane Service, Charity Hospital in New Orleans, and Hotel Dieu from January, 1946, to July, 1950.

Seasonal Incidence

The incidence according to month for this series as well as for a series from Hotel Dieu is shown in Fig. 4. The greatest number of abortions occurred in May. In an attempt to explain this springtime increase the expected date of delivery of these patients if abortion had not supervened was estimated. This was compared with the monthly rate of deliveries at Charity Hospital and at Hotel Dieu. These too demonstrated a seasonal variation with the greater number of deliveries occurring in the early autumn. From a study of Fig. 5 one may conclude that the high incidence in the spring is probably related to the greater incidence of pregnancies at that time.

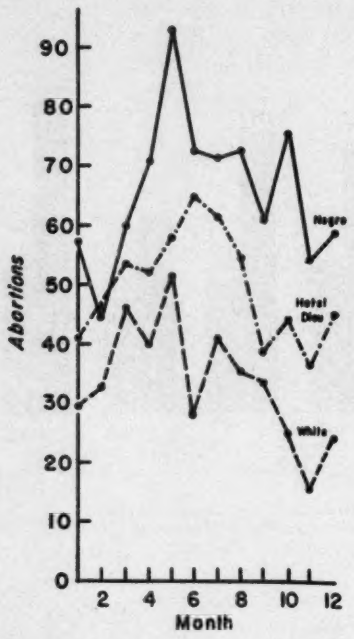

Fig. 4.—Incidence of abortions according to month in Negroes and whites in this series and in a series from Hotel Dieu covering the same period.

Age

There was no significant difference in the ages of the white and Negro patients. The majority of abortions occurred in patients between the ages of 20 and 35 years. The extreme ages were 11 and 48 years in the Negroes and 14 and 45 years in the white.

Previous Pregnancies

The relation of abortions to previous pregnancies again was similar for both white and Negro. Fig. 6 shows that most of these abortions occurred during the third, fourth and fifth pregnancies. Most patients in this series had had no previous live births (Fig. 7). Among the white patients in this series there had been 2,001 pregnancies (including the present abortions) with only 966 live babies, or 48 per cent of the pregnancies. This figure is much lower than that generally reported. Among the Negroes there had been 3,951 pregnancies with 2,022 live births, or 54 per cent.

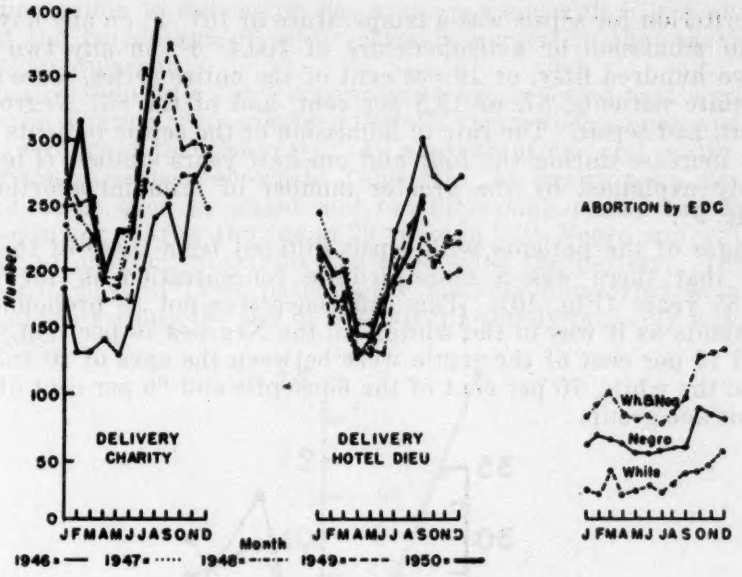

Fig. 5.—Comparison of monthly incidence of deliveries at Charity Hospital and Hotel Dieu with expected date of delivery in present series of abortions.

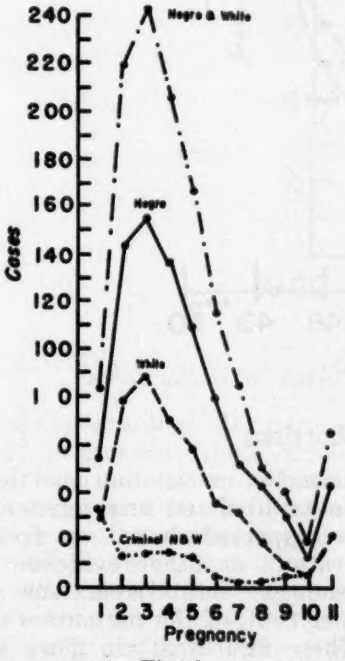

Fig. 6.

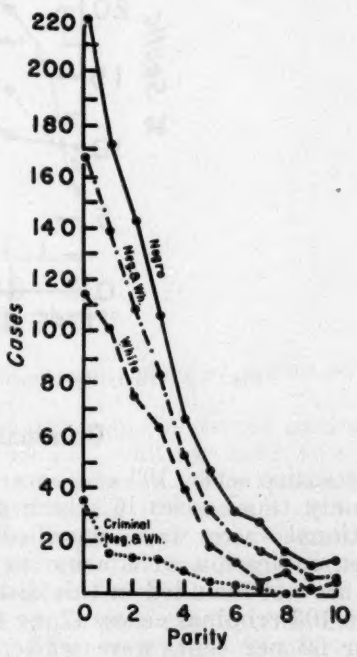

Fig. 7.

Fig. 6.—Relation of abortions to previous pregnancies in present series.
Fig. 7.—Parity of patients in present series according to color yearly.

Septic Abortions

The criterion for sepsis was a temperature of 101° F. on any day including the day of admission or a temperature of 100.4° F. on any two successive days. Two hundred fifty, or 19 per cent of the entire series, were septic. Of the 447 white patients, 87, or 19.5 per cent, and of the 857 Negroes, 163, or 19 per cent, had sepsis. The rate of admission of the septic patients has shown a distinct increase during the four and one-half years studied (Fig. 8). This is probably explained by the greater number of criminal abortions in this group (Fig. 9).

The ages of the patients with sepsis differed from those of the nonseptic group in that there was a more definite concentration in the age group of 20 to 35 years (Fig. 10). This difference was not as pronounced in the Negro patients as it was in the white. In the Negroes 70 per cent of the nonseptic and 76 per cent of the septic were between the ages of 20 and 35 years, whereas in the white, 70 per cent of the nonseptic and 86 per cent of the septic were in this age group.

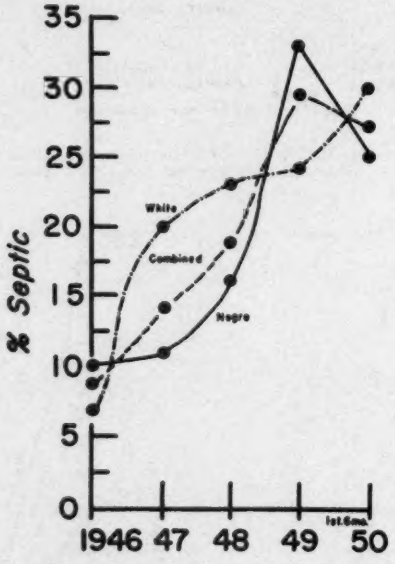

Fig. 8.—Yearly incidence of sepsis in present series.

Criminal Abortions

In the entire series 103 cases were classified as criminal abortions. These included only those cases in which patients admitted interference. Twenty-two additional cases were classified as suspected, based on fresh cervical lacerations, indication of uterine perforation, or other evidence of trauma but these are not included in this discussion of criminal abortions.

Of the 103 criminal cases, 42, or 40 per cent, of the patients were Negroes and 61, or 60 per cent, were white. These figures attain more significance when it is recalled that there were twice as many Negro admissions as white. This discrepancy is most likely explained by the fact that it is obviously difficult to obtain a history of interference from any of these patients. The seasonal incidence for the four years followed the general pattern for the whole series. The yearly incidence of criminal abortions for the period studied showed an increase from 2.8 per cent of all abortions in 1946 to 14.1 per cent

in 1950 (Fig. 9). Whether this denotes a true increase or only better history taking is impossible to determine but a comparison with Fig. 8 showing the increase in the percentage of septic cases is suggestive that the increase is more real than apparent.

Analysis of the septic cases according to age revealed that a greater proportion of the Negroes were younger than 25 years whereas more of the white women were younger than 30 years. An analysis of age and parity according to color of the patients is shown in Table III. As can be seen, most of these women had never been pregnant and the increasing parity corresponded to the increase in age. After the age of 20 years in both Negro and white women, the number of criminal abortions increased with the pariety. This is to be expected since most of these patients are younger unmarried women and in the older, married group the size of the existing family probably was the determining factor.

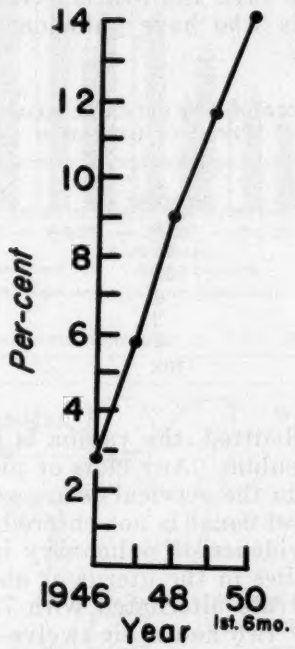

Fig. 9.—Percentage of criminal abortions in septic group of present series.

Most of the criminal abortions (91.6 per cent) occurred during the first trimester of pregnancy, these women usually waiting until two menstrual periods had been missed before seeking interference. The incidence of abortions in the respective months of gestation for all 103 cases is shown in Table IV. In those patients who revealed the method of interference, 56 white patients, or 91 per cent, and 30, or 70 per cent, of the Negro patients stated that it was either a pack or a catheter or both.

In the white group, 55, or 90 per cent, were septic, and in the Negro group, 37, or 88 per cent, were septic. These represent 63 per cent and 22 per cent, respectively, of the white and Negro septic cases. It seems obvious that many more of the septic cases must have been induced.

Treatment

The treatment of abortions on the Tulane service at Charity Hospital has varied in principle only slightly since 1930. The present treatment of

TABLE III. DISTRIBUTION OF AGE AND PARITY OF CRIMINAL ABORTIONS ACCORDING TO COLOR

AGE (YEARS)	PARITY	WHITE	%	NEGRO	%
15-19	0	4	100	7	87.5
20-24	0	9	43	7	43.7
25-29	0	9	43	1	11.1
25-29	3+			7	77.7
30-34	0	1	8.3		
30-34	2	4	33.3		
30-34	3+	7	58.3	4	80.0
35-	4+	3	100		

incomplete, complete, and septic abortions (Fig. 11) differs from former treatment only in the use of chemotherapy, antibiotics, number of transfusions, and ligation of the inferior vena cava and ovarian veins in patients with suppurative pelvic thrombophlebitis who have pulmonary infarction or who do not respond to medical therapy.

TABLE IV. INCIDENCE OF 103 CRIMINAL ABORTIONS ACCORDING TO MONTH OF GESTATION

MONTH OF GESTATION	NUMBER	%
1	16	15.7
2	43	41.6
3	35	34.3
4	6	5.6
5	2	1.8
6	1	0.9
Total	103	99.9

When the patient is admitted, the vagina is inspected under sterile precautions with a bivalve speculum. Any clots or pieces of tissue in the vaginal canal are removed. Those in the cervical os are gently extracted by means of sponge forceps. The cervical canal is not entered. In the septic cases roentgenograms are made for evidence of pulmonary infarcts, pneumoperitoneum, or radio-opaque foreign bodies in the uterus or abdominal cavity. Oxytocics, usually $\frac{1}{640}$ grain of Ergotrate alternated with $7\frac{1}{2}$ minims of Pitocin intramuscularly, are given every two hours for twelve doses. If bleeding persists, the vagina is again inspected and usually more clots and tissue are found in the vagina and cervix. Should the patient continue to bleed, dilatation and curettage are performed in the operating room.

Septic cases are managed in the same way but in addition sulfonamides and antibiotics are given and the patient is closely observed for evidences of peritonitis, abscesses, or suppurative pelvic thrombophlebitis. Dilatation and curettage are never done in these patients until signs of sepsis have completely disappeared and then only if bleeding is so severe that it is absolutely necessary to cure the uterus to prevent exsanguination. Of the 250 patients with sepsis, only 3 (1.2 per cent) required dilatation and curettage; all 3 were seen in 1946. Uterine douching or packing is not employed. In this series, 67 of the 1,054 nonseptic patients had dilatation and curettage on the initial admission. This represents 7.5 per cent of the patients with nonseptic incomplete and complete abortions admitted.

The incidence of *dilatation and curettage* for the entire series was 5.4 per cent. Twelve patients, or 4.8 per cent of the septic cases, required ligation of the inferior vena cava and ovarian veins for suppurative pelvic thrombophlebitis. This represents 44.4 per cent of the 27 cases of suppurative pelvic thrombophlebitis encountered in this series.

Blood transfusions were used liberally. The indications were shock, low hematocrit, low red blood count and/or low hemoglobin value. Transfusions were given to 310 patients, of whom 201 were Negroes and 109 were white; this represents 23.7 per cent of all patients admitted. Five hundred ninety-six separate transfusions were recorded on the patients' records. Each patient received an average of 945 ml. of blood. The largest number of transfusions given to any one patient was 7. Reactions followed 38 of the 596 transfusions, or 6.3 per cent of cases; this included 4 cases of lower nephron nephrosis. No deaths were directly or remotely traceable to transfusion reactions.

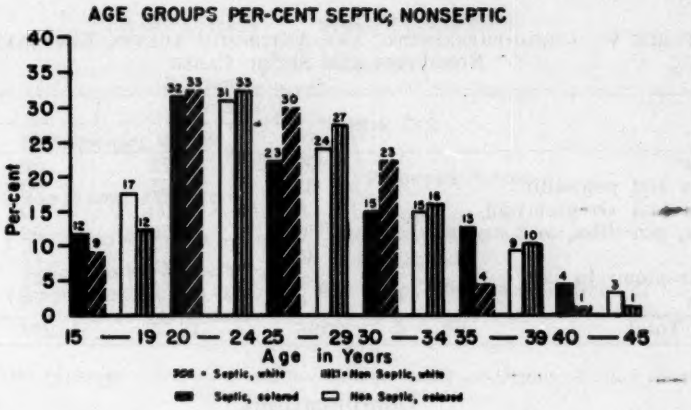

Fig. 10.—Incidence of sepsis and nonsepsis in 1,304 abortions according to age.

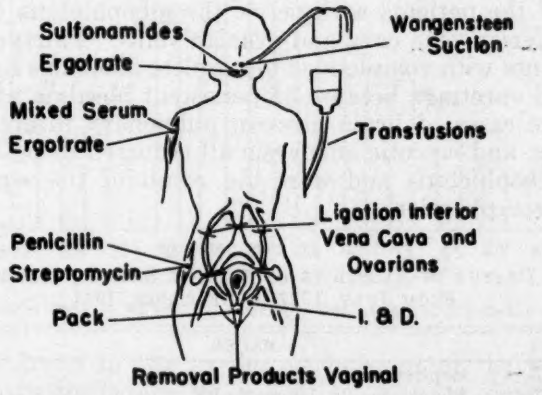

Fig. 11.—Schematic representation of method of treatment of abortions on Tulane Service, Charity Hospital in New Orleans.

Mixed serum (tetanus antitoxin, gas bacillus antitoxin) is given intramuscularly to all patients known or suspected of having had interference. One hundred seventy-nine patients (13.7 per cent) received mixed serum. Sensitivity was recorded in 12 of the 179 cases, an incidence of 6.7 per cent. There were no instances of tetanus or Welchii infection developing in any of these patients after administration of the prophylactic antitoxin and no deaths were attributable to antitoxin sensitivity. In 2 patients, tetany was present on admission.

Sulfonamides and *penicillin,* and more recently *streptomycin,* were given liberally to those with sepsis and to many of the patients not considered to

have sepsis by the criterion employed. Penicillin was given only to the most seriously ill until 1948 after which its employment was generous. Streptomycin began to be used widely early in 1949. Aureomycin was beginning to be used early in 1950. The individual choice of drug and dosage depended upon the availability and the clinical response. Blood, uterine, cervical, and vaginal cultures were so inconclusive that choice of drug based upon types and sensitivity of organisms was impractical. Table V shows the chemotherapeutic and antibiotic agents used in the two principal types of cases. Of the cases in which these agents were not used, 81.21 per cent were nonseptic and 4.4 per cent septic.

TABLE V. CHEMOTHERAPEUTIC AND ANTIBIOTIC AGENTS EMPLOYED IN NONSEPTIC AND SEPTIC CASES

	NONSEPTIC		SEPTIC	
	NO.	%	NO.	%
Sulfonamides	92	8.72	50	20.00
Sulfonamides and penicillin	63	5.97	93	37.20
Sulfonamides and streptomycin	0	0.00	0	0.00
Sulfonamides, penicillin, and streptomycin	6	0.56	62	24.80
Penicillin	33	3.13	12	4.80
Penicillin, streptomycin	4	0.37	22	8.80
Streptomycin	0	0.00	0	0.00
Total	198	18.75	239	95.60

Complications

The complications of abortion are sepsis and hemorrhage and complications thereof. Fig. 12 shows the type of complications encountered in this series. Twelve of the patients with pelvic thrombophlebitis (44.4 per cent) had ligation of the inferior vena cava and ovarian veins. Thirty-nine (3.2 per cent) of the 1,197 patients with complete or incomplete abortions had to be readmitted for dilatation and curettage because of persistent bleeding after discharge from the hospital. The cases of brain abscess, pulmonary infarction, subacute bacterial endocarditis, and mycotic aneurysm all occurred in patients with suppurative pelvic thrombophlebitis and were the result of the septic embolism characteristic of that complication.

TABLE VI. DEATHS IN ABORTIONS ON TULANE SERVICE, CHARITY HOSPITAL, FROM JULY, 1937 TO DECEMBER, 1941

NO.	YEAR	CAUSE	SERVICE
1	1937	Septicemia	Gynecologic
2	1937	Shock due to hemorrhage	Medical
3	1938	Tetanus (admitted in tetany)	Surgical
4	1938	Sepsis, peritonitis, pelvic abscess	Gynecologic
5	1939	Sepsis	Gynecologic
6	1939	Peritonitis, pelvic abscess, bronchopneumonia	Gynecologic
7	1939	Peritonitis, bronchopneumonia, gangrenous appendix, abortion	Medical
8	1939	Hemorrhage, anuria	Gynecologic
9	1940	Sepsis, uremia	Gynecologic
10	1940	Peritonitis	Gynecologic
11	1940	Sepsis, pneumonia (hypostatic)	Medical
12	1940	Tetanus (admitted in tetany)	Surgical
13	1940	Pulmonary infarct, sepsis, hepatic abscess	Gynecologic
14	1941	Pulmonary infarct, sepsis	Gynecologic

Mortality

In the present series of 1,304 cases, there were 6 deaths (0.46 per cent).* The mortality rate for abortions at Charity Hospital has been considerably reduced in recent years, as evidenced by a comparison of the deaths for an earlier period of 54 months ending Dec. 31, 1941, during which there were 14 deaths (1.04 per cent) in 1,346 women with abortions admitted to the Tulane Service. During this latter period there were 3,881 patients with abortions admitted on all services at the hospital with 42 deaths (1.08 per cent). During the period covered by this study 59 deaths were reported in Louisiana as due to abortions; the mortality rate by year is shown in Fig. 13.

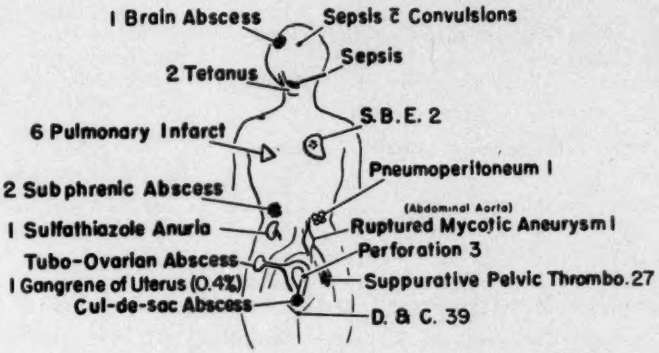

Fig. 12.—Schematic representation of complications in 1,304 abortions, Tulane Service, Charity Hospital in New Orleans.

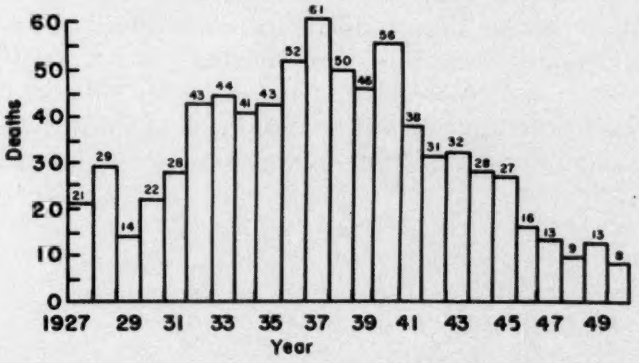

Fig. 13.—Yearly mortality rate in cases of abortion for state of Louisiana from 1927 to 1949.

The causes of death in the earlier period and in the period covered by this study are shown in Tables VI and VII. The six deaths in the present series represent all deaths from abortion on the Tulane Medical and Surgical Services at Charity Hospital. Two of the patients had suppurative pelvic thrombophlebitis and ligation was done too late to prevent fatal complications from the multiple septic emboli. The two patients with tetanus failed to respond to the present method of treatment. The patient with anuria due to self-medication with sulfonamides was subjected to renal decapsulation and treated on the medical service. Present methods of treatment might have prevented her death. The one patient with sepsis who died in the admitting room was in the hospital two and one-half hours (no autopsy was obtained). The two patients who died subsequent to 1946 were moribund on admission.

*Between 1946 and 1949 there were 11,661 term deliveries on the Tulane Obstetrical Service at Charity Hospital with 18 maternal deaths, an uncorrected mortality rate of 0.16 per cent.

TABLE VII. DEATHS IN CRIMINAL ABORTIONS, TULANE SERVICE, CHARITY HOSPITAL, FROM JANUARY, 1946 TO JULY, 1950

YEAR	CAUSE	SERVICE	REMARKS
1946	Suppurative pelvic thrombophlebitis, peritonitis, pulmonary infarct, subacute bacterial endocarditis, criminal abortion.	Gynecologic	Penicillin, 1,420,000 u. prior to vena cava ligation; died 1 month after ligation
1946	Suppurative pelvic thrombophlebitis, bacterial endocarditis, mycotic aneurysm aorta, criminal abortion	Gynecologic	Penicillin, 930,000 u. prior to vena cava ligation; died 3 months after ligation
1946	Tetanus, criminal abortion (admitted in tetany)	Gynecologic	Penicillin, 150,000 u.; tetanus antitoxin 160,000 u.; died 6 days after admission
1946	Anuria, uremia due to sulfonamide, criminal abortion	Gynecologic	Self-medication, renal decapsulation; died on medical ward
1949	Criminal abortion, sepsis	Admit	Admission temperature 105° F. (rectal), convulsion; died in 2 hours, 25 minutes
1950	Criminal abortion, tetanus (admitted in tetany)	Surgical	Gynecologic consultation; tracheotomy; tetanus antitoxin; died in 24 hours

Summary

An analysis of 1,304 cases of patients with abortions admitted to the Tulane Gynecologic Service of Charity Hospital of Louisiana is presented. The seasonal variation in the incidence of admissions with a peak in May correlated with the seasonal incidence of pregnancies. Two hundred fifty of the cases were septic. Six of these patients died, a mortality of 0.46 per cent, as contrasted with a rate of 1.06 per cent during the four and one-half years prior to 1941. This recent lowering of the mortality rate is attributed to the liberal use of chemotherapy and antibiotics, the availability of blood for transfusions, and recognition and prompt treatment of complications.

PAIN AND PAIN RELIEF IN ESSENTIAL DYSMENORRHEA

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THIS article deals with the problem of menstrual pain, its pathogenesis and relief. It is the preliminary report from a research program at New York University and at this stage is based upon experience with 800 students.

The research dealt mainly with the pain in "essential" dysmenorrhea, i.e., the menstrual pain without traceable anatomical pathology. All patients with gynecological findings ("secondary" dysmenorrhea) were referred for gynecological treatment, either through their private physicians or through channels of the Medical School. Still there remained the great majority of patients, those with "primary" or "essential" dysmenorrhea, and the Department was confronted with the need for its relief and, if possible, prevention.

Material

All freshmen with menstrual pain reported their disturbance in their health records. Admission to the program was voluntary; besides, we excepted all those with "secondary" dysmenorrhea and those whose disturbance was under medical treatment. As a result, the program worked with an average of 160 new freshmen a year, 640 in four years. In addition, it was consulted by older students and personnel of the University.

With regard to age groups, this means: 640 individuals in the age groups from 16 to 19 years (with a preponderance of 17 and 18), and 150 in their twenties.

In the interest of the pain research, the case records of the program listed the following items:

Pertinent facts of personal and family history; history of individual cycle and its past disturbances; essence of medical examination; neurological examination with special attention to the autonomic constitution; evaluation of developmental status; psychological evaluation; time table of cycle, bleeding, and pain.

With regard to the *pain* itself: First appearance and changes of the pain in previous menstruations; its character—whether coliclike spasms, dull ache, or however described by the patient; its location; its timing with regard to onset and quantity of bleeding; finally, its response to medication (not analgesics) with known and selected physiological tendencies. These pharmacological studies on the pain became an essential part of the program.†

The gynecological status of the case load was normal, because all individuals with pathological or even dubious findings were excluded from the program. The duration of individual follow-up, partly influenced by academic technicalities (semester, vacations, etc.) varies from about 6 months to 4 years, with emphasis on the longest possible time-spans.

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†The hormones used in this research were largely supplied by the clinical research division of the Schering Corporation, Bloomfield, N. J.

The Role of Psychoneurosis

The old explanation of dysmenorrheal pain had been relatively simple: Whenever the gynecological findings were negative, the complaints were ascribed to a greater or smaller degree of psychoneurosis. Today we know that this concept was wrong.

The changes appearing in menstruation are basically caused by chemical (hormonal) factors. This chemical stimulation, production, quantity, and proportion of its components, varies greatly in different individuals; in addition, individuals vary in their autonomic response to the same stimulus.

These great individual differences are found in individuals with entirely normal gynecological status. In our experience, they are not the exception but the rule. And they account for severe clinical disorders, even without the concurrence of any psychogenic disturbance.

Tested with the necessary care, the etiological significance of psychoneurosis was surprisingly low in our students' group at New York University. Psychoneurosis was neither a typical symptom nor even particularly frequent in the group. This was established by the current case work and by additional controls.

Health records of 300 students with "menstrual pain" were compared with records of 300 students who stated their menstruation as "normal." (These records contained all previous illness, listed by the student, and the findings of the Department's medical examination.) The health records of the students with dysmenorrhea showed no more traces of psychoneurosis than did the records of the controls. In more than 60 per cent "menstrual pain" was the *only* disturbance, past or present, which the student listed (in contrast to the multitude of complaints which is frequent in the health records of psychoneurotics).

Patients who had been considered psychoneurotic because of the violence of their menstrual reactions were calm and well poised after specific medication (not analgesics). This effect, however, could not be achieved by control medication, which was identical in size, taste, and color of coating, but different in contents.

It is true that in a number of cases the psychogenic overlay prevails in the clinical picture. But the other extreme is just as typical: cases in which severe autonomic cramps are borne with silent heroism, because the patient has been told that she is healthy and that her condition is "normal." This second type is less noisy and therefore less commonly known; but it is very frequent in primary dysmenorrhea, and the pain is often underrated.

The clinical picture of primary dysmenorrhea is composed of a true somatic disorder and its varying psychogenic overlay. This does not minimize the usefulness of psychological treatment; but it calls above all for knowledge and treatment of the underlying physical disorder.

Individual Autonomic Response

A study of the physical disturbance which causes cyclic pain in essential dysmenorrhea required consideration of three factors: the nature of the chemical stimulus, the nature of the local reaction which is provoked by the stimulus and causes the pain, and the individual sensitivity to stimulus, local reaction, and pain.

We started from the third factor, the differences of individual sensitivity. Aside from the mentioned psychological side, many physical factors had to be considered.

In the first 300 patients, we traced all recognizable factors in physical constitution, development, and clinical findings which could account for differences of the periodic pain reaction. To summarize the result: No single factor proved pathognomonic by itself.

It is true that underdevelopment plays an etiological role, as is shown by the frequency of adolescent dysmenorrhea. But this role is neither as simple nor as constant as one may assume. There were patients with all physical symptoms of hormonal underdevelopment, including an infantile gynecological status, whose cycle had been normal and painless for years (while there was proof that this painlessness was not due to anovulatory menstruations). And there were patients with a mature physique and a mature and healthy gynecological status, who went through years of severest menstrual pain. Yet in both groups, certain individuals were promptly relieved by medication of estrogenic hormone, others did not respond to it at all.

Similar observations were made in cases with aftermaths of Fröhlich's syndrome (19 in our first group of 300 patients). This condition showed no characteristic features with regard to either menstrual pain or its relief by estrogenic hormone.

Body "types" played altogether no role; they were as varied as in the control groups. While some of our patients were asthenic, the great majority were normally strong individuals, who were very healthy during the interval but very sick during the first day of the menses. Nor was the metabolism characteristic. Here, too, we found all possible differences, and the majority of the patients had a normal basic metabolic rate.

Particular attention was paid to conditions of increased autonomic spasticity. It was possible that a "vagotonic" constitution, i.e., a disposition to parasympathetic hyperreaction, played a special role in primary dysmenorrhea. Such a disposition is easily diagnosed; it shows in family and personal history by its relation to asthma, hay fever, gastric disturbances, and "nervousness," and may have characteristic clinical symptoms, intestinal and, particularly, neurovascular. The question was: Are such cases frequent in a large case load of primary dysmenorrhea, and do they show peculiarities in the monthly pain?

The answer was negative in both respects. First, the percentage of such cases was low in our group with dysmenorrhea, not higher than in any control group with normal menses. Second, during the menses, such patients had increased symptoms from their autonomic disturbances, for instance from gastric pain or a mucous colitis; but they did not have pelvic cramps of particular strength. Altogether, we came to the conclusion that a general disposition to parasympathetic spasticity has no specific influence upon the physiological mechanism which causes the menstrual pain. This conforms with therapeutic experiences. Medication which has a specific effect upon parasympathetic spasms has in general no specific effect upon menstrual pain (with the exception of plain anesthetics and narcotics). This holds particularly for the belladonna group. Atropine sulfate, if given without supportive analgesics, was altogether ineffective in our case load.

Briefly, no factors were found in physical constitution, development, gynecological, medical, or neurological status, which could be considered pathognomonic or predisposing.

The Effect of Estrogenic Hormone

At this stage of the research, at which no conclusive explanation could be found for cause and nature of the pain, we started to examine the only "specific" pain relief which was known in primary dysmenorrhea, the effect of

estrogenic hormone. We used Schering's Estinyl (ethinyl estradiol) in tablet form, and the observations reported in the following were obtained with this preparation. After variations in dosage and timing, we used it as follows:

Beginning from the first day after the end of the preceding menstruation, one tablet of Estinyl, 0.05 mg., was taken every day, for 10 to 12 subsequent days. This technique seemed clinically most effective. We often saw success from less (10 or 8) tablets, and in all cases gave no more than one tablet a day.

If the medication was effective, the pain relief was obvious in the subsequent menstruation. In this case, the medication was repeated in from 3 to 5 intervals, often in diminishing doses. When the the treatment was entirely ineffective the first time, repeated attempts were usually of no avail.

Undesired side effects were remarkably few. (This refers to a case load of young patients whose general health had been previously checked.) In 300 cases of medication, there was one case of allergic exanthema; 15 patients reported discomfort, mainly nausea, which promptly disappeared when the medication was discontinued or the dosage diminished. In no case was the disturbance serious or lasting. The question of the time table and of anovulatory menstruations will be discussed below.

Estrogenic hormone prevented the pain in about 60 per cent of our cases with essential dysmenorrhea (i.e., in about 180 of the 300 patients to whom it was given). No other medication had a comparable effectiveness.

The term "prevented" was used because in most of these patients the previously severe pain was not only alleviated, but the menstruation was described as "practically painless" or just "painless." Many of the patients stated independently that they had been surprised by the bleeding and not been prepared for it, because for years they had been forewarned by hours of pain before the onset, while this time there was no pain before or afterward.

This clinical effect is so strong that it would seem to solve the entire problem, were there not one obstacle: Upon the pain of the other 40 per cent of the patients the hormone has no effect at all. In these cases, there was not an "insufficient" pain relief, but there was no pain relief whatsoever. Besides, once the hormone had been ineffective at the first attempt, it was practically useless to try it again in the next interval; for the outcome remained the same. This contrast between success and failure of the hormone medication is so obvious in a large case load that one comes to realize that there must be a physiological difference between the two groups, which plays a role in the pain problem.

Before following this lead, we dealt with the question to what extent the painlessness after hormone medication was due to anovulatory menstruations. To our present knowledge, a surplus of estrogenic hormone may prevent the maturing of an ovum, and the resulting anovulatory menstruation may be painless. Therefore it seemed important to decide whether the pain relief by estrogenic hormone could be achieved only in anovulatory cycles.

Since the usual method of proof, endometrial biopsy, was not feasible in a case load of healthy students, we used other methods to answer the question: temperature curves and—more conclusively—the timing of medication. While in general we avoided estrogen medication in the second half of the interval, we gave it to a series of patients intentionally after ovulation, i.e., in the latter part of the interval and after a normal ovulation had been sufficiently evidenced by its clinical symptoms, including characteristic temperature curves.

The results showed that the two factors are not interdependent. The hormone produced pain relief also in ovulatory cycles. This was learned from patients whose menstruations had been persistently painful without hormone medication, whose ovulation was sufficiently certain several days before the hormone was given, and in whom the next menstruation was relieved.

Clinically, this question was less important than we thought at first, because all irregularities which we observed during estrogen treatment were limited to the phase of the treatment itself. During the months of estrogen medication, the time table may be irregular, the interval prolonged or shortened, the bleeding diminished. But after the treatment was discontinued, the regular schedule was invariably restored. This was seen in all these patients, many of whom have been treated two and three years ago, and some of whom have married and gone through normal pregnancies in the meantime. Briefly, the patients considered the hormone treatment beneficial, and no harm has been reported afterward.

What causes the difference between the patients whose pain responds to estrogenic hormone and those in whom it does not? Notwithstanding all clinical symptoms, there was no ready answer to this question. It was not a difference of gynecological status; this status was normal in both groups, and patients with juvenile, narrow cervices were found in both. It was not a traceable difference in constitution or development, in medical or neurological findings. All these features were approximately the same in both groups.

Only in a general sense can it be stated that the pain relief by estrogenic hormone is most likely to occur in young and immature individuals, and least likely in older and married persons; but even this statement is not exclusive and does not explain the difference in pain relief.

To approach the question from another angle, we treated those patients who did not respond to estrogen with progesterone.

Effect of Progesterone

From statements in the literature, we had hoped that a certain number of our patients would be relieved by progesterone medication, just as others had been relieved by estrogen. But so far all our attempts have failed.

Since some publications on the success with progesterone in dysmenorrhea were too definite to be disregarded, we were long inclined to ascribe our failure to technical differences of application.

Due to the nature of our case load, only oral application was practicable. With this limitation, however, the medication was tried systematically and with many variations in dosage and timing. We used Pranone tablets (10 mg.) in the second half of the interval. When smaller doses showed no effect, they were increased up to 30 mg. per day in ten subsequent days, i.e., up to 300 mg. between ovulation and bleeding. In other cases, this total was given in three days preceding menstruation, including its first day. The results were always the same: There was no undesirable side effect, in fact, no clinical effect, and no influence upon the menstrual pain. We then combined progesterone with estrogen medication, with again no noticeable effect on the part of progesterone.

To summarize: In a series of 60 patients, we did not see any pain relief in dysmenorrhea by oral application of a well-tested progesterone preparation, given in amounts of 80 to 300 mg. in the second half of the interval. The discrepancy between these negative results and the positive results of other authors cannot yet be explained.

What Causes the Pain?

All our experiences led back to the basic question of what actually causes the pain in primary dysmenorrhea. Quite aside from the problem of the stimulus, there must be a local process which causes pain, and this process must be definable in terms or physiology.

It had been a great step forward when gynecology rejected mere mechanical explanations (such as a slight retroversion or narrowing of the cervical canal) on one side, mere hysteria on the other. Neither explanation had furnished effective treatment.

Ever since, the accepted theory has been the assumption of painful uterine spasms, comparable, in a general way, with an intestinal colic or with minor labor pains. The analogy with spasms of other organs with autonomic nerve supply would make this explanation likely and logical.

However, the longer we worked on this premise, the more we were confronted with clinical contradictions. This pain had features which did not fit into the physiological chapters of either intestinal spasms or labor pain. The first contradiction was its response to medication.

Pharmacological peculiarities had to be expected, in view of the specific chemistry of the female reproductive organs. We thus mentioned that autonomic antispasmodics had little influence upon menstrual pain, in many cases none. But another observation seemed more peculiar: In many patients the pain responded more readily to salicylates and barbiturates than to Demerol and even opiates. In fact, several patients who did not respond to Pantopon responded promptly to Empirin. At first, we dismissed such reactions as psychoneurotic, but when they recurred, and in stable and reliable patients, they seemed to conflict with the features of an abdominal colic or an abdominal organ spasm.

The greatest doubt, however, was caused by the time table of the pain. As mentioned, we had recorded the time table of the pain in its relation to the bleeding. Thereby we could trace the connection between pain and bleeding in over 500 cases. The results seemed remarkably inconsistent with the theory of uterine muscle spasms as the cause of menstrual pain.

There was no definite connection between the beginning of pain and bleeding. The pain started hours or minutes before the onset of the bleeding, or together with it, or minutes or hours afterwards. (In many cases, these intervals were much greater.) The theory of a primary mechanical obstruction (e.g., by a narrow cervix), which had to be overcome by painful muscle spasms, could be early discarded, because in more than half of the cases the pain started minutes or hours after the flow had started and become regular.

About 60 per cent of the patients described their pain as "cramps" and coliclike; 40 per cent described it as a more constant ache. But even the "cramps" were not accompanied or followed by changes in the quantity of the flow. Altogether, pain and flow were described as remarkably independent of each other. This was very different from the symptomatology of muscle spasms for the expulsion of contents.

These facts, together with the mentioned clinical and pharmacological observations, made us feel that the pain was not caused by spasms of the uterine wall, at least not in the great majority of our patients.

After dismissing this theory, we scrutinized other processes which accompany the onset of menstruation. In doing so, we were impressed by a physiological factor, which is likely to cause pain, fits the time table, and is free from the mentioned clinical contradictions. This factor is the vasoconstriction, the angiospasm of endometrial arteries, which begins from 24 to 4 hours before the bleeding, lasts through its onset, and is later supplemented by alternating phases of vasoconstriction and vasodilation.

These vascular reactions were found by the basic research of Markee (published from the Carnegie Institute in Washington in 1940). With regard to their details we refer to Markee's publications (ref.), and to the description of the vascular reactions in Novak's textbook (1948).

The significance of these vascular findings and their role in menstrual bleeding are still being debated. The vasoconstriction may well be instrumental in the necrosis of the mucous membrane, i.e., the physiological objective of menstruation, the renewal of the inner lining of the uterus. Whether it is the main cause of this necrosis or, as is maintained by other authors (Smith and Smith, Kaiser), chemical and metabolic processes play a more basic role in it, is not yet conclusively decided. It seems likely, however, that chemical and vascular theories will supplement rather than contradict each other, as has been the experience with "spontaneous" vasoconstrictions in other parts of the body.

Neurologically, a simpler conclusion seems permissible. This proved angiospasm of endometrial arteries may well cause menstrual pain. For this it has many precedents in the body: "spontaneous" pain, which is caused by angiospasm and/or the resulting arterial ischemia which leads to necrosis. In fact, most of the mentioned contradictions, pharmacological and others, disappear, if one works on the premise of an angiospasm, which is proved, rather than of uterine muscle spasms, which have never been quite substantiated in primary dysmenorrhea.

On this basis, we examined the condition with vasodilatory medication.

Therapeutic Attempts With Vasodilatory Medication

Many vasodilatory drugs are also strong antispasmodics; they had to be avoided, in order to differentiate between vascular effects and antispasmodic effects upon the uterine musculature. For this reason, we discontinued a therapeutic series of 50 cases which in 1946, we had treated with nicotinic acid and nicotinamide. The effects had been promising in some cases; but due to the antispasmodic components of both medicaments, the results could not answer the vascular question.

In a subsequent series of 80 patients we used the hormone Padutin, which has a specific vasodilatory effect yet, from previous laboratory and clinical tests, a negligible effect upon the musculature of the human uterus. Although newer vasodilators were available, Padutin was chosen because of its proved clinical harmlessness, which seemed important in a case load of young and sensitive patients. Since 1948, it has been given in more than 80 cases without any undesirable side effect.

Padutin* is a vasodilatory insulin-free hormone gained from the pancreatic gland. It has a marked vasodilatory effect, combined with a practically complete absence of clinical side effects.

For several months we were concerned that a vasodilator, if given during menstruation, might cause hemorrhages; therefore we gave it in small doses and only before the onset of the flow. Both precautions, however, proved unnecessary: even in large doses and given repeatedly during menstruation, the medicament did not increase the flow. The best dosage seemed to be two tablets (of 10 units each) three or four times a day, starting early on the day of pain or, if the patient could time it, the day before.

The pain relief was good in some cases, partial in others, but absent in more than 50 per cent of the patients. (Notwithstanding its use in 80 cases, statistics cannot yet be given, because we started with too small doses and varied dosage and timing with growing experience.) Altogether the pain relief was neither as frequent nor as complete as that with estrogenic hormone.

At this stage of our studies we learned from the literature that Griffith and Little have seen pain relief from medication with Priscoline. Since the chemical constitution of Priscoline is very different from that of Padutin yet

*Produced and tested in the early 1930's in Germany, it is manufactured in the U. S. by Winthrop-Stearns, Inc.

both are specific vasodilators, this conformed with our working theory that the vasoconstriction played a role in the pathogensis of primary dysmenorrhea.

Priscoline is the far stronger vasodilator, and the statistics which Griffith and Little report from their Priscoline treatment of 28 patients seem correspondingly better than were our experiences with Padutin in 80 cases. On the other hand, Priscoline has uncomfortable and rather severe side effects, particularly tachycardia and vomiting, which we could not and cannot risk in our case load of young students. As mentioned, we chose Padutin, in spite of its relative weakness, because of the absence of any such side effect.

In their present form, neither Padutin nor Priscoline can be recommended for general use as ideal pain relievers in dysmenorrhea. The one is not strong, the other not innocuous enough. Whether either of them will be modified or supplemented to be reliable and harmless in general practice remains to be seen. What matters in both, however, is that a vasodilator rather than a general antispasmodic seems to have a specific effect upon the pain in certain forms of essential dysmenorrhea.

How this pain relief by a vasodilator is related to the pain relief by estrogenic hormone cannot yet be decided on the basis of our experiments. There is much clinical and experimental evidence, however, that the estrogenic hormone contains a vasodilatory factor and the luteum hormone a vasoconstricting factor. Both factors may well exist in addition to and independently of the spasmodic and antispasmodic effects which the two hormones exert upon the uterine musculature.

The anovulatory menstruation takes place without a new corpus luteum, hence without the normal surplus of progesterone. Yet, as far as we know, the anovulatory menstruation is always painless. This painlessness comes about in a cycle with diminished progesterone production, i.e., with a preponderance of estrogen; in this it corresponds to the painlessness which is obtained by estrogen medication.

To what extent these sensory effects are due to vascular reactions and the details of these reactions are questions of our current research. It is certain that the vascular reactions and their role in the pain problem must be distinguished from reactions upon the uterine musculature. In this respect it is noteworthy that the vasodilatory effect of estrogenic hormone has been recently used for relief of angiospasms in other parts of the body.

Summary

A research program on the pain of essential dysmenorrhea, its pathogenesis and prevention was set up at New York University and has worked with 800 students over a period of four years. Results obtained so far:

1. Psychoneurosis was no more frequent in this case load with essential dysmenorrhea than in control groups with normal menses.

2. No organic factors were found in physical constitution, development, medical, neurological, and gynecological status which could be considered pathognomonic or predisposing. Disposition to increased autonomic spasticity was no more frequent than in the control groups. Where present, it had no appreciable bearing upon the menstrual pain. General antispasmodics were throughout ineffective.

3. In a series of 300 patients, estrogen medication produced full pain relief in 60 per cent, had no effect upon the other 40 per cent. The reason for this difference is still unknown. Pain relief by estrogen medication was also obtained in ovulatory cycles.

4. Progesterone produced no pain relief in a series of 60 patients.

5. The physiological cause of the pain was investigated in 800 patients. The previous theory of coliclike spasms of the uterine musculature was abandoned for the great majority of cases. In many patients, the pain seemed to be caused by an angiospasm of uterine arteries, and responded to vascular rather than antispasmodic medication. It is assumed that a vasodilatory factor, contained in or activated by the estrogenic hormone, plays a role in the painlessless of normal menstruation, and that its deficiency is a frequent cause of essential dysmenorrhea. Attempts are being made to identify this factor.

Conclusion

It is not yet possible to point out one single physiological factor as the cause of all forms of essential dysmenorrhea; nor is it possible to decide whether any such single factor exists. A more limited conclusion, however, seems permissible at this stage.

There is a frequent form of essential dysmenorrhea, particularly in young and underdeveloped patients, which belongs not in the chapter of uterine muscle spasms and their abdominal colic, but in the chapter of "angiospasms," caused by chemistry. It is due to an unbalance of chemical stimulation and seems to yield to specific medication.

At this stage, it is assumed that the painlessness of normal menstruation requires a vasodilatory factor which is contained in the estrogenic hormone or activated by it, and that deficiency of this factor causes essential dysmenorrhea in many young individuals. In our current therapeutic series attempts are being made to identify this factor.

This work is being done in the Department of the University Physician, Dr. John E. Sawhill, to whom the writer feels greatly indebted for his constant interest and cooperation. In the gynecological field the author wishes to express his gratitude to Dr. Benjamin Watson of the Columbia College of Physicians and Surgeons and to Dr. Barbara Logan of the Woman's Hospital in New York, who assisted the program with their valuable advice. Acknowledgment is likewise due to the Medical Research Division of the Schering Corporation.

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TUBAL STERILIZATION; A REVIEW OF 1,169 CASES

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DURING recent years 12 patients who had been sterilized at the University of Iowa Hospitals by the Madlener technique are known to have become pregnant. These failures stimulated this study in which the records of all patients sterilized were reviewed in regard to indications, the various techniques employed, the morbidity, and the end results of operation. An attempt was made to follow each patient by personal interview or letter, and was successful in 68 per cent. The remaining 32 per cent were considered to have been successful since failures of this nature usually are brought to the attention of the institution or surgeon.

Various Methods of Tubal Sterilization

Since 1930, the Madlener method has been employed almost exclusively at the University Hospitals, because of its simplicity and the excellent results reported elsewhere. Madlener,[1] in 1919, first described his technique of tubal sterilization. A loop of each tube is grasped with forceps and crushed at its base with a broad clamp. Each arm of the loop is ligated with nonabsorbable suture at the point of crushing.

Bishop and Nelms[2] later described the method used by Pomeroy who made no claim to its originality, but stated he had never seen it used before. In this method, the base of a loop of tube is tied with catgut and the loop is excised distal to the point of ligation.

Cornual resection was popularized at Johns Hopkins Hospital and has been widely accepted. Peitmann[3] ligated the tube with silk at two places 2 cm. apart, split the peritoneum of the tube, excised that portion between the ligatures, and sutured the peritoneum over the defect with silk. Rabinowitsch[4] employed the same technique as Peitmann except that he buried the uterine end of the tubes in the myometrium. Köhler[5] modified the Madlener method by excising the loop distal to the point of ligation. Hofbauer[6] severed the tube, ligated the uterine end with silk, and approximated the round and ovarian ligaments over the stump. Planner[7] devised the method of doubly ligating the tube with silk, excising that portion between the ligatures, and burying the proximal stump in the broad ligament. Birch[8] employed a method which differs from the technique of Planner only in that he dissected the tube and placed the ligatures in apposition to the muscularis rather than the serosa. Russell[9] described a method of doubly ligating the tube with catgut, excising the loop, and burying the ends in the broad ligament. He believed that subsequent restoration of tubal patency and function would be possible. Ries[10] described a modification of cornual resection in which the bladder peritoneum is sutured to the raw surface of the uterus in order to bury the site of resection. Aldridge[11] reported a reversible

method of burying the fimbriated ends of the tubes in the broad ligaments. Russell,[9] and Rubovits and Kobak[12] have published good résumés on the history of tubal sterilization.

Material

Between January, 1926, and July, 1948, 1,169 operations were performed at the University Hospitals on the Fallopian tubes for the primary purpose of producing sterilization. Tubal sterilization was the only operative procedure performed in 502 cases, while in the remaining 667 instances some other surgical procedure was done.

TABLE I. INDICATION FOR STERILIZATION

	GROUP A	GROUP B
Uterine prolapse and vaginal relaxation	137	148
Recommended by State Eugenics Board	26	167
Late pregnancy toxemia or hypertensive vascular disease	115	80
Two or more cesarean sections	89	89
First cesarean section plus some other indication	7	2
Epilepsy and mental deficiency	46	4
Psychosis	24	9
Diabetes	4	3
Multiparity	37	0
Cardiac disease	34	33
Tuberculosis	16	16
Renal disease	18	14
Ectopic pregnancy	6	2
Previous unsuccessful attempt at sterilization	1	7
Organic neurologic lesion	17	2
Miscellaneous	7	9
	584	585

Table I enumerates the various indications for sterilization in this series. The cases, for purposes of comparison, have been divided into two groups. The first, or Group A, comprises 584 cases from January, 1926, through May, 1940; and the second, or Group B, comprises 585 patients who were sterilized from June, 1940, through June, 1948. This purely arbitrary division was designed merely to determine whether over the years there has been any essential change in the clinical philosophy underlying attempts to limit procreation by surgical means.

Operations to correct uterine prolapse and relaxations of the pelvic floor with concurrent steriliation presented the greatest number of cases (285). Some plastic procedures were done partially to justify sterilization in grand-multiparous patients in whom social factors were the principal indication. Under an old Attorney General's ruling, sterilization is illegal in Iowa except on the basis of medical indications; social and economic conditions are not considered legitimate. However, in certain instances where only borderline medical indications existed, socioeconomic factors weighted the decision in favor of sterilization. Such cases are listed under the prevailing medical indications.

Sterilizations for other than obstetric and gynecologic conditions were carried out only on the written recommendation of the department primarily concerned with the clinical condition obtaining; those in which the indication originated within the departmental field were decided upon in conference. The consent of the patient was, of course, obtained.

Indications

The data in Table I show certain differences in the weighting of various indications over the years. Before the Board of Eugenics began to function in

1934, women with mental or nervous conditions were referred for sterilization by the hospital department primarily concerned; later such patients were referred to the Board which then "ordered" the procedure on eugenic grounds. Multiparity, as such, was occasionally an acceptable indication up to the time of the Attorney General's ruling; thereafter it was not listed. In the second period (Group B) there were fewer sterilizations for late toxemia and hypertensive vascular disease, in spite of the admission of more patients with those diagnoses. The reason for this more recent less radical attitude is not clear, although it may be related to the better acceptance of contraceptives and to greater reliance on antepartum supervision to protect those women in any subsequent pregnancies. A common indication for sterilization has been two or more cesarean sections. In recent years, because of the greater safety of abdominal delivery, there has been a tendency not to sterilize a patient unless she has had at least three cesarean sections. Eight patients with unsuccessful tubal sterilizations were subsequently subjected to a second operation for sterilization and are listed in Table I under the indication of "Previous Unsuccessful Attempt at Sterilization" even though the original reason for limiting childbearing was still present.

TABLE II. INDICATIONS FOR STERILIZATION

	GROUP A	GROUP B
Organic Neurologic Lesions.—		
Multiple sclerosis	7	1
Previous laminectomy	0	1
Polyneuritis	3	0
Headaches	1	0
Chronic encephalitis	1	0
Optic atrophy	1	0
Huntington's chorea	3	0
Parkinson's disease	1	0
Miscellaneous Lesions.—		
Dermoid cyst	1	1
Diaphragmatic hernia	0	1
Osteomalacia	1	1
Goiter (permanent tracheotomy)	0	1
Laparotomy and multiparity	0	2
Hemophilia carrier	0	1
Acute yellow atrophy of liver	0	1
Lung abscess	1	0
Bronchiectasis	1	0
Carcinoma, rectum	1	0
Repeated congenital anomaly	0	1
Asthma	1	0
Sacroiliac relaxation	1	0

Table II is self-explanatory except for the one patient sterilized for "sacroiliac relaxation." This occurred early in the series when most lower back pain was ascribed to loosening of that joint; in all probability, the incapacitating pain, aggravated by pregnancy, was due to herniation of a vertebral disc or to some such other unrecognized entity.

The average age at the time of the operation was 29.5 years. The youngest patient was 13 and the oldest was 50 years. The average parity was 3.8. One-hundred eighteen women were nulliparous. Most of these were referrals from the State Board of Eugenics. Parity was not recorded in 28 cases.

Postpartum Sterilization

There is no agreement among physicians as to the best time to perform puerperal sterilization. This decision is more controversial than the type of sterilization or the justification for the procedure. Skajaa,[13] in 1932, published the first report on postpartum sterilization. Since his patients were not limited to those with uncomplicated deliveries, his morbidity was higher than expected. Among 58 women operated upon between the fifth and twenty-ninth postpartum days, there were 7 cases of thrombosis and 1 of embolism.

Adair and Brown,[14] in 1939, advocated that postpartum sterilization be performed during the first 24 hours. Their morbidity rate was 12 per cent in 50 cases. They emphasized the importance of operating only upon patients with uncomplicated deliveries. Diamond[15] reported 63 sterilizations done on the day of delivery with a morbidity of 3.2 per cent (2 cases). Hewitt and Whitley[16] performed 100 operations for sterilization within one hour after spontaneous delivery with a morbidity of 2 per cent. Pfuetze[17] reported 73 women operated upon within 12 hours after delivery with a morbidity of 12.7 per cent. Whitacre and associates,[18] carried out bacteriologic examinations on puerperal women and found 80 per cent of uteri infected 10 hours after delivery and all contaminated by the second day. In their opinion all puerperal sterilizations should be done within the first day after delivery. Russell[9] claims that the danger of thrombophlebitis and embolism increases greatly when sterilizations are done after the first postpartum day. Hellman[19] found histologic evidence of acute salpingitis in 24 per cent of patients sterilized from the fifth to the tenth postpartum days, but in only 2.4 per cent of those operated upon before the fifth day. He was unable to demonstrate that the patients who showed acute salpingitis were the ones who exhibited morbidity.

On the other hand, Knight,[20] Goldblatt,[21] and other workers have emphasized the importance of observing the early puerperium for febrile reactions before performance of sterilization. Thornton and Williams[22] reported 309 puerperal sterilizations with a morbidity of 21 per cent. They found no correlation between the time of operation and morbidity, but of 12 patients operated upon the first day, only one was morbid. Lock and co-workers[23] reported 30 puerperal sterilizations done on the fourth and fifth days with only one morbid patient.

During the years of this study it has been the policy of the University Hospitals to perform sterilizations after a few days of observation have demonstrated an afebrile puerperium. Two hundred seven interval abdominal Madlener sterilizations were performed with a morbidity of 6.8 per cent. During these same years, 200 similar operations were done during the puerperium with a 9 per cent morbidity according to the standards of the American Committee on Maternal Welfare. Altogether 407 abdominal Madlener operations have been done in these two groups with a morbidity of 7.6 per cent.

Table III shows the postoperative morbidity according to the time of operation after delivery. Only 6 per cent of the postpartum sterilizations were done during the first two days of the puerperium. There was a relatively high morbidity when the sterilizations were done on the third, fourth, and fifth days. In a control group of puerperal women having no sterilization, most elevations of temperature occurred on the first, third, fourth, and fifth days (Table IV). Therefore, in some of the morbid cases, the superimposed sterilization cannot be definitely blamed for the fever. In none of the postpartum sterilizations was the fever high enough or of sufficient duration to cause much concern. The highest temperature in the entire group was 101.6° F. and lasted only 3 days. The longest postoperative hospital stay was 15 days.

TABLE III. RELATION OF MORBIDITY OF 200 ABDOMINAL STERILIZATIONS TO DAY OF PUERPERIUM WHEN PERFORMED

DAY OF OPERATION DURING PUERPERIUM	NO. OF CASES	NO. OF MORBID PATIENTS	PERCENT OF MORBIDITY
1	1	0	0.0
2	11	1	9.1
3	8	1	12.5
4	18	3	16.7
5	21	3	14.3
6	23	0	0.0
7	21	1	4.8
8	16	0	0.0
9	11	1	9.1
10	17	2	11.8
11	14	2	14.3
12	11	0	0.0
13	7	1	14.3
14	6	1	16.7
15-30	15	2	13.3
Total	200	18	9.0

TABLE IV. MORBIDITY OF 430 CONTROL POSTPARTUM PATIENTS DURING 1947 AND 1948

DAY OF PUERPERIUM		NO. OF MORBID PATIENTS
1		8
2		2
3		10
4		8
5		5
6		3
7		4
8		4
Percentage of morbidity	10.2	44

Vaginal Sterilization

Von Graff[24] recommended the vaginal approach in performing tubal ligations. While there are advantages in this method, such as the absence of a visible scar, and the convenience when performing vaginal plastic repairs, there are certain disadvantages. Vaginal tubal ligation is often technically more difficult than abdominal sterilization and is impossible in the early puerperium; even in nonpuerperal patients there is a greater risk of injuring other pelvic organs, and of causing bleeding difficult to control. In 78 vaginal Madlener sterilizations performed as interval procedures and unassociated with other plastic surgery, there were 9 febrile patients (11.5 per cent). One of these women developed a pelvic abscess which necessitated surgical drainage. At the present time, in this clinic, vaginal ligations are seldom done except as a part of some plastic operation for the correction of prolapse or vaginal wall relaxations.

There is no agreement concerning the effect of appendectomy upon postoperative morbidity, when it is carried out as an elective procedure during laparotomies for other reasons. In the entire group of 407 abdominal Madlener sterilizations, the morbidity rate was 7.6 per cent, whereas in 28 cases in which appendectomy was also done, the morbidity was 10.7 per cent. Thornton and Williams,[22] however, report a series of 176 cases of appendectomy combined with sterilization with no higher morbidity than in simple sterilization.

Results of Sterilization

While results of other types of sterilization have been reported, only those of the Madlener and Pomeroy methods have been extensively reviewed. The

popularity of these two has been due to their technical simplicity and their excellent results as compared with those of other methods. Knight[20] surveyed the literature up to 1946 and in a later article[25] reviewed 4,952 Madlener and 1,262 Pomeroy sterilizations with an incidence of failure of 0.6 per cent and 0.3 per cent, respectively. Lull[26] recently reported 1,550 Pomeroy operations with four failures (0.2 per cent). The exact Pomeroy technique was not used in 2 of the failures.

TABLE V. RESULTS OF VARIOUS TYPES OF STERILIZATION

PROCEDURE PERFORMED	NO. OF PATIENTS	FAILURES	PERCENTAGE OF FAILURES
Madlener (abdominal)	544	4	0.7
Madlener (abdominal with cesarean section)	194	4	2.0
Madlener (vaginal)	377	4	1.1
Cornual resection (abdominal)	40	0	0.0
Cornual resection (abdominal)	7	0	0.0
Pomeroy (abdominal)	3	0	0.0
Salpingectomy	3	0	0.0
Defundation	1	0	0.0
	1169	12	1.0

Among 1,169 tubal sterilizations performed in this clinic, there were 12 known failures, an incidence of 1.0 per cent. Table IV shows the various methods of sterilization employed and the failures associated with each. In addition to the 12 definite failures there were 5 other patients who gave menstrual histories compatible with early abortion. Although only 54 sterilizations were done by methods other than the Madlener technique, there were no failures in this group. There was no significant difference in the results obtained by the abdominal over the vaginal approach. However, sterilization done at the time of cesarean section resulted in 2 per cent of failures as contrasted with 0.7 per cent when not associated with abdominal delivery.

There were 5 deaths among the 1,169 women subjected to sterilization (0.4 per cent). Two of these deaths followed cesarean section, two occurred after major surgical procedures with incidental tubal ligation, and one was the result of the disease for which sterilization was done. In retrospect, it is doubtful if this patient should have been sterilized. In none was the cause of death directly attributable to sterilization.

A short history of each of the 5 patients who died follows:

1. L. P., Hospital No. E 9002, 30 years of age, gravida v and para v, had a normal delivery on May 9, 1951. On the sixteenth postpartum day a trachelorrhaphy, perineorrhaphy, ventral suspension, and appendectomy were done under ethylene anesthesia. Because of epilepsy with mental deterioration bicornual resection was done for sterilization. The patient had a febrile course and died on the fifteenth postoperative day from bilateral lobar pneumonia.

2. B. K., Hospital No. C 5792, 20 years of age, gravida iv and para iv, had a second classical cesarean performed on July 21, 1931, under ethylene anesthesia. A Madlener tubal ligation was done at the same time. The postoperative course was febrile and the patient died on the fifth day because of bronchopneumonia and pelvic peritonitis.

3. M. D., Hospital No. K 14962, 41 years of age, gravida iv and para iv, was operated on June 20, 1935, under ethylene anesthesia. Because of relaxation of the vaginal walls, dilatation and curettage, amputation of the cervix, and an interposition operation with Madlener ligation of the tubes were performed. The patient had a febrile course and died on the fifth day from generalized peritonitis.

4. C. B., Hospital No. 40-8716, 40 years of age, gravida x and para iv, was admitted to the hospital on June 28, 1940. She gave a history of having had bilateral renal calculi with recurring attacks of pyelonephritis for 13 years. Examination revealed her to be four months pregnant. An abdominal hysterotomy with tubal Madlener ligation was done on July 1, 1940, under local anesthesia. The patient died on Aug. 7, 1940, from kidney failure.

5. E. K., Hospital No. 43-11206, 26 years of age, gravida ii and para ii, had a second classical cesarean with a Madlener ligation on Oct. 23, 1943, under spinal anesthesia. The patient was discharged from the hospital on the thirteenth day after having had an afebrile puerperium. She died at her home two days later from pulmonary embolism.

Of the 12 patients who had unsuccessful Madlener sterilizations, five were delivered subsequently by cesarean section; one of these had also had a spontaneous poststerilization abortion; four delivered vaginally, one twice; one was subjected to hysterotomy at the third month of gestation; one had an early spontaneous abortion; and another had an ectopic pregnancy.

Eight of the 12 patients whose sterilization operations were failures were subsequently reoperated upon at the University Hospitals. In 2 instances, serial sections of the removed tubes revealed one tube patent with nonabsorbable suture material still present, and in a third case both tubes were open. In 2 patients, at least one tube appeared to be normal but the tubes were not probed and no serial sections were made. In another case, a sound could be passed from the abdominal end of one tube to its isthmus. No accurate observations could be made in two patients because of adhesions. All 12 patients were resterilized by Madlener ligation, cornual resection, or salpingectomy.

Comment

Sampson[27] in his study of postsalpingectomy endometriosis, or, as he called it, "endosalpingiosis," has offered a plausible explanation for many failures of tubal sterilizations. He believed that the traumatized endosalpinx behaved differently during its regeneration from the mucosa of other hollow organs under similar conditions. He stated that "tubal epithelium grew after healing was complete and invaded the muscularis." Many gynecologists of experience have seen instances of unusual proliferation of tubal epithelium, especially in the formation of fistulous tracts between the abdominal wall and uterus after salpingectomy. It is not difficult to understand how canalization might take place or how an epithelized tract could form after tubal sterilization. Fuchs and Lork[28] also believed that the tube had unusual regenerative powers and described an instance in which the tube regenerated completely after partial subserous excision. In his case serial sections showed only slight atresia of the muscularis. Silk is notorious for its propensity to cut through devitalized tissue and form sinuses. Numerous instances[17, 29] are recorded in which these processes have resulted in failures of sterilization.

In the Pomeroy method the most important step in the procedure is to ligate a rather large loop of tube. The absorbable ligature is primarily for hemostasis. Postoperatively the muscle in the tubal wall retracts and the redundant peritoneum helps seal off the stumps. In the Madlener method careful attention must be given to the size of the loop, the degree of crushing of the loop, and the tightness of the ligature in order to insure success. The process of muscle retraction might well cause failure after the Madlener procedure. Nürnberger[30] showed that, in unsuccessful ligation of the tube, the muscle atrophies under the suture and retracts to both sides, so that the ligature ultimately encloses only the serosa and mucosa and its constricting action is appreciably decreased.

Summary and Conclusions

One thousand one hundred sixty-nine tubal sterilizations are reported with 12 known failures (1.0 per cent). The Madlener technique was employed in 1,115 cases and all the known failures were in this group. Vaginal sterilization has the same incidence of failure as abdominal, but is technically more difficult and carries a slightly higher morbidity. Tubal ligation at the time of cesarean section resulted in 2 per cent failures.

The morbidity of postpartum sterilization is not significantly affected by the day on which it is carried out during the puerperium. The chief advantage of early postpartum sterilization is the shortening of the patient's hospitalization.

Due to a higher number of failures than was felt justified, the Madlener technique has been discontinued except for sterilizations done during vaginal plastic procedures. The Pomeroy method is currently the procedure of choice in other patients.

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THE EXCRETION OF CREATINE AND CREATININE DURING PREGNANCY

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IT WAS established[1-9] years ago that creatine is usually found in pregnancy urine. Subsequently, very little effort has been made to determine either its exact quantitative variation or the significance of its excretion during pregnancy. Quantitative data for the excretion of creatinine are similarly sparse.

The present study was undertaken, with the use of modern methods and instruments, in an attempt to establish normative data for the excretion of creatine and creatinine and to determine the nature and possible significance of their variation.

Methods

Twenty-four hour urine samples were collected from mothers regularly enrolled in the Institute's research program. All of the pregnancies were normal and uncomplicated as judged by regular medical and laboratory examinations. The subjects, nearly all above average intelligence, were carefully instructed in the methods of urine collection and the importance of their cooperation. The urine samples were collected in light-proof bottles and were refrigerated during or immediately after the period of collection. Aliquots which could not be immediately analyzed were preserved with toluene in the cold or frozen without preservative.

Aliquots were analyzed for creatine and creatinine by a modification[10] of the Jaffé picric acid method, for ketosteroids by continuous hydrolysis and extraction[11, 12] with the use of the Holtorff and Koch colorimetric procedure,[13] and for thiamine.[14]

Blood samples, taken by venipuncture after the basal metabolism test, were analyzed for hemoglobin,[15] vitamin A and carotene,[16] and alkaline phosphatase.[17, 18] Basal metabolism determinations were conducted by measurement of the time required for the consumption of 1 L. of oxygen, with the use of the Jones machine,[19] while the subject was in the postabsorptive state. Dietary intake records were collected in alternate two-week periods and analyzed by the method of Sontag and Wines.[20, 21]

Observations

Creatinine Excretion.—Table I reveals the normal data obtained by the analysis of 283 urine samples from 37 normal pregnant women. Means, ranges, and standard deviations are given as a basis for appraising the degree of deviation, or abnormality, of any urinary value. Fig. 1 shows that the distribution of creatinine follows a symmetrical curve and that therefore the use of the standard deviation, as an expression of variability, is acceptable.

One would expect to find an increased excretion of creatinine during pregnancy, based upon the fact that the synthesis of creatinine by the fetus (and placenta) would be additive. This is apparently not the case, although it must be admitted that a 5 kilogram fetus would form only an additional 0.10 Gm. of creatinine per day, an amount which would be difficult to determine with assurity even in a population of this size. Since the creatinine does not increase, the creatinine coefficient (Table I), based upon the body weight of the mother, appears to drop during pregnancy. In fact, it drops proportionately to the increase in weight of the mother. The data suggest, therefore, that either most of the new tissue formed during pregnancy does not form creatinine or that some kind of "compensatory" change in creatinine formation or utilization occurs. Perhaps creatine storage in the uterus, placenta, and fetus accounts for this finding. At any rate, a somewhat lower creatinine coefficient near the end of pregnancy is to be regarded as normal.

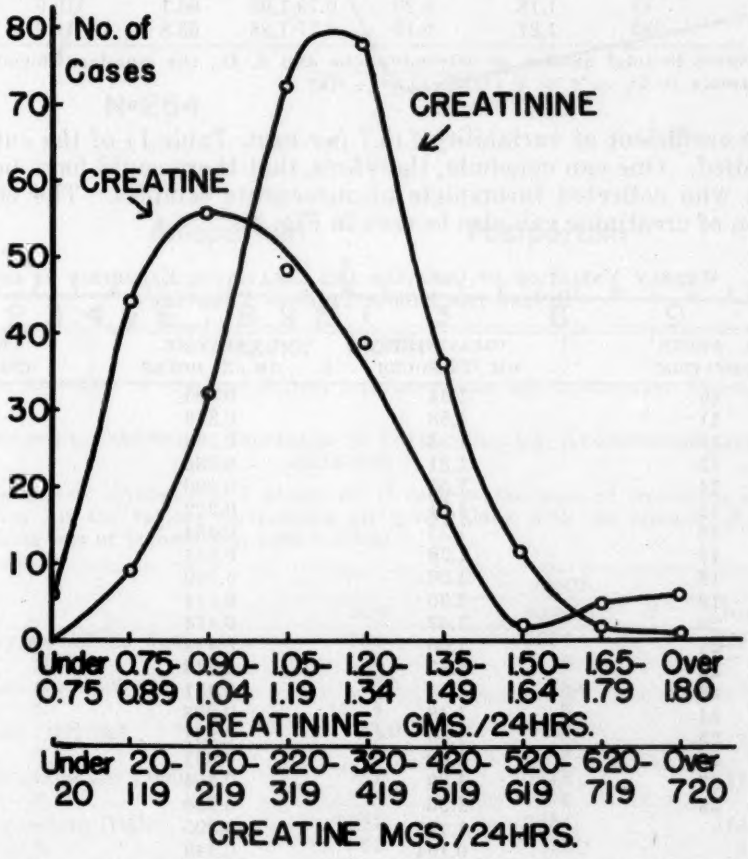

Fig. 1.—Distribution of the urinary excretion of creatinine and creatine during pregnancy.

The creatinine coefficient of 21.0 obtained for maturing girls[22] agrees substantially with that found here for mothers.

Table II represents the analyses of 19 samples taken at weekly intervals from a subject who conscientiously collected very accurate 24-hour urine specimens. The excretion of creatinine during this time varied between 1.26 and 1.60 Gm. of creatinine with a mean of 1.41 and a standard deviation of 0.19. The coefficient of variability (S. D./M) of 13.7 per cent is but very little smaller

TABLE I. EXCRETION OF CREATININE DURING PREGNANCY

LUNAR MONTH	N*	CREATININE MEAN GM./24 HR.	CREATININE S. D.* GM./24 HR.	CREATININE RANGE GM./24 HR.	BODY WEIGHT (KILOGRAMS)	CREATININE COEFFICIENT MEAN MG./24 HR./KG.	CREATININE COEFFICIENT S. D.* MG./24 HR./KG.
3	8	1.31	0.22	1.01-1.54	59.6	22.1	1.8
4	12	1.14	0.13	0.87-1.37	58.8	19.5	3.1
5	23	1.23	0.16	0.96-1.64	61.7	20.1	2.7
6	31	1.24	0.20	0.88-1.88	62.5	19.8	2.6
7	33	1.22	0.16	0.97-1.65	63.0	19.6	2.6
8	39	1.24	0.19	0.78-1.65	65.1	19.2	2.9
9	37	1.20	0.18	0.77-1.62	65.5	18.4	3.1
10	59	1.18	0.19	0.83-1.59	67.8	17.8	3.1
Subtotal	242	1.21	0.18	0.77-1.88	64.4	19.1	3.0
Post partum							
1.5	22	1.12	0.18	0.78-1.56	60.4	18.7	3.1
12	19	1.25	0.21	0.80-1.66	59.8	21.2	3.1
Subtotal	41	1.18	0.20	0.78-1.66	60.1	19.9	3.3
Total	283	1.21	0.19	0.77-1.88	63.8	19.2	3.1

*N refers to total number of determinations and S. D., the standard deviation, is based on the formula S. D. $= \sigma = \sqrt{(1/N)\ (\Sigma X^2) - Mx^2}$

than the coefficient of variability (15.7 per cent, Table I) of the entire population studied. One can conclude, therefore, that there could have been but few subjects who collected incomplete or inaccurate samples. The constancy of excretion of creatinine can also be seen in Fig. 3.

TABLE II. WEEKLY VARIATION OF CREATINE AND CREATININE EXCRETION OF ONE INDIVIDUAL DURING THE MIDDLE THIRD OF PREGNANCY

NO. WEEKS' GESTATION	CREATININE GM./24 HOURS	CREATINE GM./24 HOURS	CREATINE CREATININE
10	1.34	0.065	0.04
11	1.58	0.373	0.25
12	1.38	0.162	0.12
13	1.31	0.282	0.22
14	1.55	0.096	0.06
15	1.54	0.202	0.13
16	1.33	0.484	0.36
17	1.36	0.484	0.36
18	1.26	0.309	0.24
19	1.36	0.174	0.13
20	1.43	0.494	0.35
21	1.60	0.414	0.26
22	1.37	0.378	0.28
23	1.51	0.451	0.30
24	1.48	0.288	0.20
25	1.40	0.231	0.17
26	1.40	0.651	0.47
27	1.29	0.354	0.27
28	1.36	0.290	0.21
Mean	1.41	0.325	0.23
S. D.	0.194	0.149	0.047
Coefficient of variability*	13.7	45.8	20.5

*Coefficient of variability = (S. D./M) × 100.

Table III indicates the fact that creatinine excretion is related to the total dietary calories as might be expected from the fact that creatinine excretion is related to body weight. The difference between the high and low group, in food consumption, as expressed in calories, is significant (P = 0.01). There seems to be no relationship to the distribution of calories between fat, protein, and carbohydrate within this population. No relation was found to hemo-

globin, plasma or dietary carotene, or to thiamine nutrition as judged by load test and diet record analyses. The birth weight of the infant of the "high" group was 3.38 kilograms and of the "low" 3.37 kilograms.

Most interesting is the fact that the excretion of 17-ketosteroids is related to the excretion of creatinine. The difference between the high and low

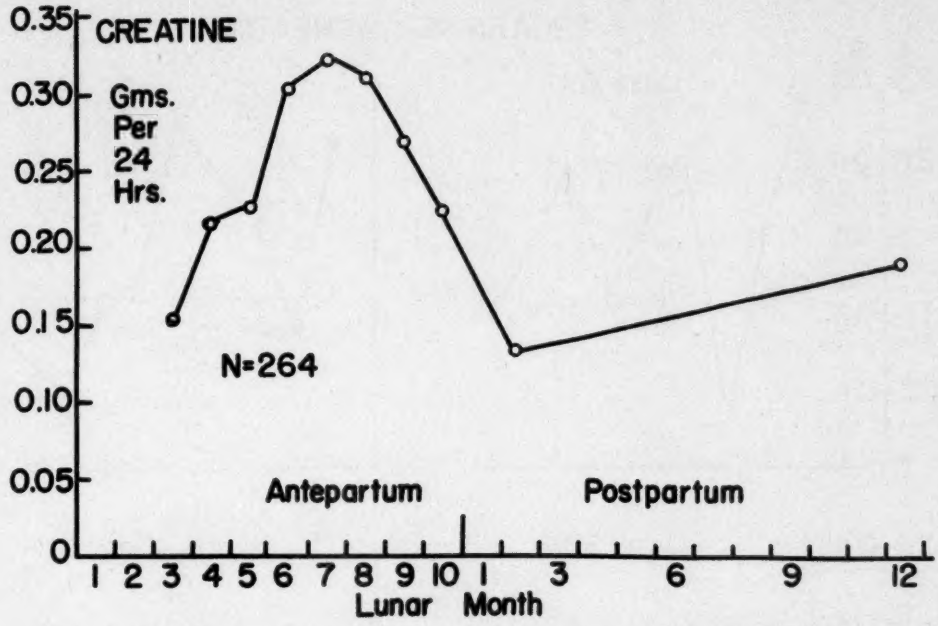

Fig. 2.—Excretion of creatine during pregnancy and the postpartum period.

TABLE III. RELATING CREATININE EXCRETION TO TOTAL CALORIES, KETOSTEROIDS, AND OTHER MEASURES

The subjects were divided into 3 groups of 12 each on the basis of creatinine excretion. The mean values for the various components are given along with the number of subjects (N) on whom both sets of information were available.

	GROUP		
	LOW	MIDDLE	HIGH
Calories per day calc. from diet	1798	1956	2223
N	8	8	6
Protein as grams per 1,000 Cal.	38.5	38.4	36.0
N	8	8	6
Fat as grams per 1,000 Cal.	41.0	39.7	42.4
N	8	8	6
Carbohydrate as grams per 1,000 Cal.	121	118	117
N	8	8	6
Calories per day output, BMR	1381	1454	1648
N	11	10	11
Body weight in kilograms	62.1	62.4	68.8
N	12	12	12
Hemoglobin as grams per 100 ml.	12.7	12.8	12.7
N	11	11	11
Plasma carotene as μg. per cent	129	192	169
N	6	5	5
Thiamine excretion per cent of 5 mg. test dose	37	30	34
N	10	10	8
Ketosteroids milligrams per 24 hours	7.95	10.3	10.7
N	12	12	12

creatinine groups is significant beyond the 1 per cent level ($P > 0.01$). A close correlation between the excretion of 17-ketosteroids and creatinine has been reported[23] for growing children. Such a correlation suggests that muscle mass, as measured by creatinine excretion, is perhaps controlled by "androgenic," or at least by 17-ketosteroidogenic hormones.

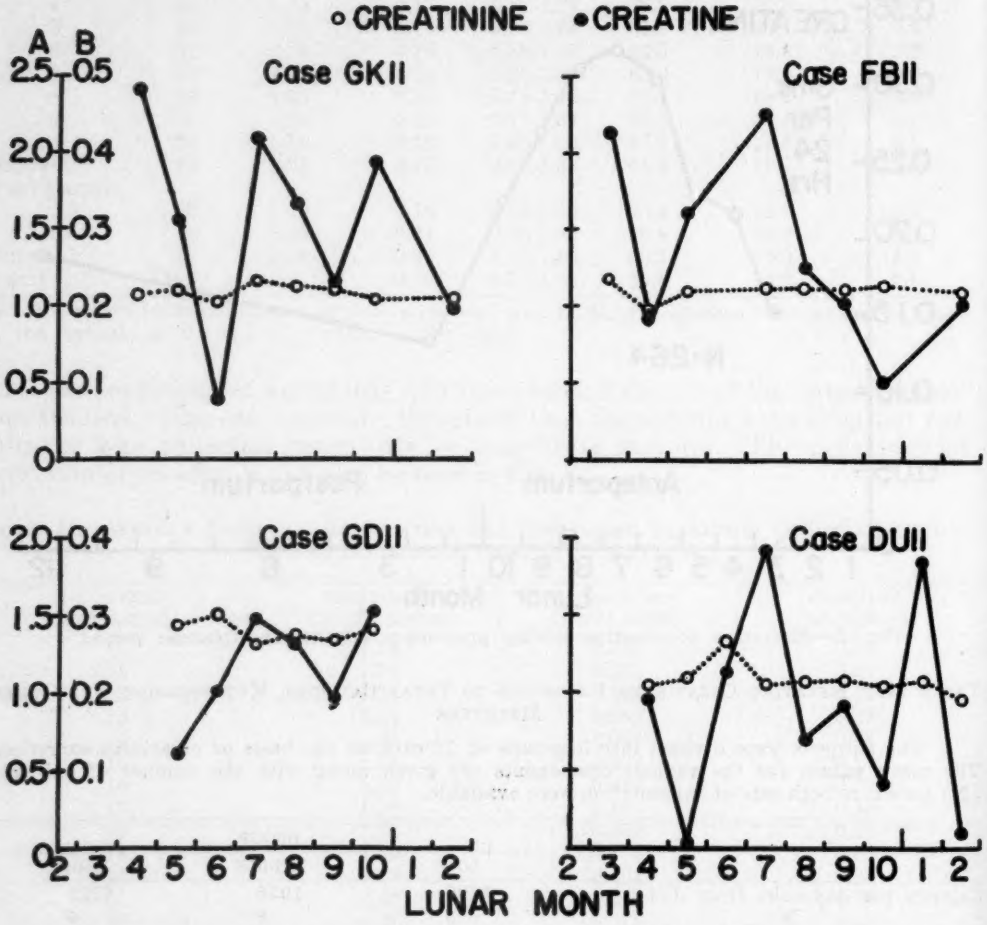

Fig. 3.—The excretion of creatine and creatinine in four cases selected at random. Scale A represents creatinine in grams per 24 hours, scale B represents creatine in grams per 24 hours. Scale B is expanded to five times that of A in accordance with the fact that the mean excretion of creatinine is five times that of creatine.

Creatine Excretion.—The data obtained from the analysis of 264 samples of urine for creatine content is given in Table IV. The distribution in Fig. 1 illustrates that the data are somewhat skewed so that the standard deviation as an expression of variability must be used with caution.

When the values are plotted (Fig. 2) it can be seen that the excretion of creatine, on the average, forms a smooth curve with a peak occurring at the seventh lunar month.

Fig. 3 represents the creatine excretion of four subjects. The remarkable variability of creatine excretion is illustrated. In spite of this month-to-month variability, however, it turns out that individuals can be meaningfully separated in terms of their mean creatine excretion. When this is done,

in order to seek possible relationships, it is found (Table V) that the basal calories output is highly related but that calorie consumption, and diet composition in terms of fat, protein, and carbohydrate are not. Blood carotene level, hemoglobin, and thiamine nutritional status are likewise unrelated.

The relation between creatinuria and total calorie output is shown graphically in Fig. 4. This finding suggests that creatinuria during pregnancy must be influenced by thyroid activity as has been shown to be the case with

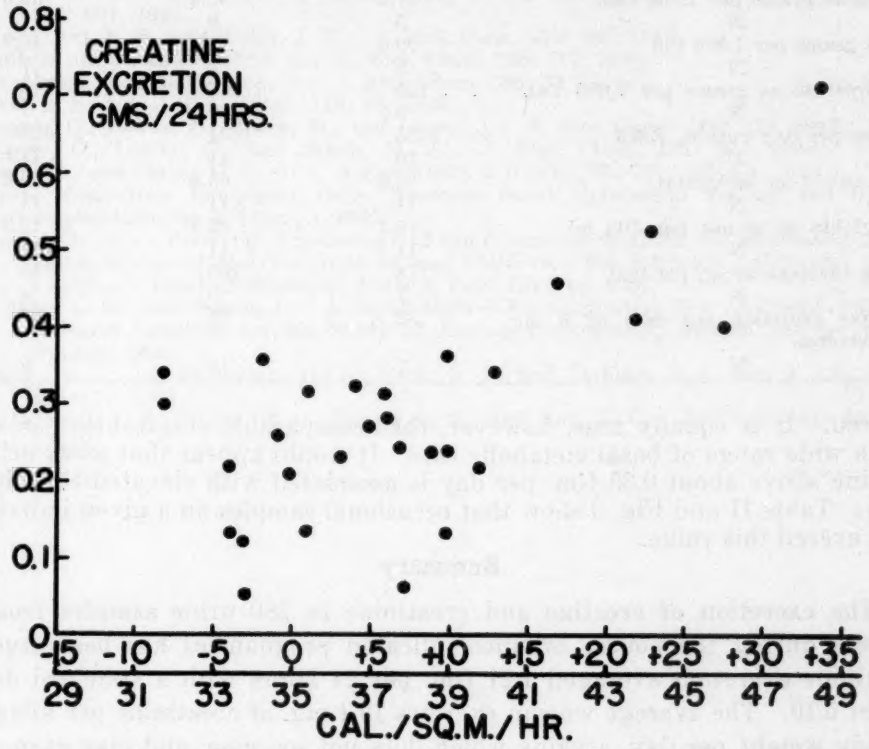

Fig. 4.—Relation between creatinuria and basal metabolic rate. The figures given above the cal./sq. m./hr. axis are percentages of the "Jones norm." This norm is estimated to be about 10 per cent too high for the Fels population.

TABLE IV. EXCRETION OF CREATINE DURING PREGNANCY

LUNAR MONTH	N	CREATINE		
		MEAN GM./24 HR.	S. D. GM./24 HR.	RANGE GM./24 HR.
3	7	.153	.17	0.009-0.426
4	11	.217	.13	0.039-0.484
5	22	.225	.16	0.005-0.743
6	29	.256	.17	0.020-0.715
7	31	.321	.19	0.020-1.03
8	35	.310	.21	0.010-1.07
9	33	.267	.16	0.038-0.728
10	55	.225	.14	0.000-0.786
Subtotal	223	.259	.18	0.000-1.07
Post partum				
1½	22	.135	.10	0.005-0.323
12	19	.202	.19	0.010-0.772
Subtotal	41	.166	.15	0.005-0.772
Total	264	.244	.18	0.000-1.07

TABLE V. RELATING CREATINE EXCRETION TO CALORIE OUTPUT AND OTHER MEASURES

The subjects were divided into 3 groups of 11 each on the basis of average creatine excretion. The mean values for the various subjects are given together with the number of subjects (N) on whom both sets of information were available.

	GROUP		
	LOW	MIDDLE	HIGH
Calories per day calc. from diet	2064	2028	1791
N	5	9	7
Protein as grams per 1,000 Cal.	37.2	37.0	39.8
N	5	9	7
Fat as grams per 1,000 Cal.	39.4	41.2	40.2
N	5	9	7
Carbohydrate as grams per 1,000 Cal.	125	117	118
N	5	9	7
Calories per day output, BMR	1455	1431	1625
N	10	11	11
Body weight in kilograms	62.5	63.9	65.6
N	11	11	11
Hemoglobin as grams per 100 ml.	12.5	12.8	12.9
N	11	11	11
Plasma carotene as μg. per cent	178	160	135
N	7	5	4
Thiamine excretion per cent of 5 mg. test dose	32	33	38
N	7	10	9

children. It is equally true, however, that comparable creatinuria can exist over a wide range of basal metabolic rate. It would appear that *mean* urinary creatine above about 0.35 Gm. per day is associated with elevated thyroid activity. Table II and Fig. 3 show that occasional samples on a given individual often exceed this value.

Summary

The excretion of creatine and creatinine in 280 urine samples from 36 subjects during the course of uncomplicated pregnancies has been studied. Creatinine excretion averaged 1.21 Gm. per 24 hours with a standard deviation of 0.19. The average woman excretes 19.1 mg. of creatinine per kilogram of body weight per day, a value which does not increase, and may even drop somewhat, during pregnancy. The average creatine excretion is 0.24 Gm. per day with values starting at 0.15 Gm. per day in the third lunar month, increasing to a peak of 0.33 at the seventh lunar month, and dropping to 0.22 by the tenth month and to about 0.15 by the first month post partum. The excretion of 17-ketosteroids is significantly higher in those women who excrete large amounts of creatinine, while the basal metabolic rate is higher in those women who excrete larger amounts of creatine. No explanation could be found for the high week-to-week variability in creatine excretion.

The authors gratefully acknowledge the technical assistance of Eleanor Clark, Werner Jacobson, and Jean Inman. The study would have been impossible without the untiring efforts of Ruth Bean in arranging for the accurate collection of the samples. Thanks are due to the mothers who cooperated so unselfishly and to Dr. L. W. Sontag, Director of the Institute, who encouraged these researches and offered valuable criticism. Lucretia Floor assisted in the dietary record analyses and Mary Davis in statistical calculations.

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PUERPERAL HYSTERECTOMY*

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(From the Margaret Hague Maternity Hospital)

HYSTERECTOMY, performed at the time of cesarean section or immediately after vaginal delivery is not a very common surgical procedure. Since it produces an abrupt cessation of childbearing and is in itself an operation of some magnitude we have reviewed such cases in the experience at the Margaret Hague Maternity Hospital. The usual indications for such an operation include: fibromyoma, uterine rupture, abruption of the placenta, placenta accreta, puerperal infection, sterilization, intractable bleeding from placenta previa, and uncontrolled postpartum hemorrhage.

Table I presents the indications which have occurred at least once each in our experience.

It will be noted that this list could be used interchangeably as a list of causes of hemorrhage in the obstetric patient. The list is by no means complete in reference to either indications for hysterectomy or postpartum hemorrhage, but will serve as a background for the discussion of the various indications.

We are not interested in the technical details of the operation but will endeavor to show that, in a rather small but significant group of cases, hysterectomy is ultimately necessary as a legitimate method of treating postpartum hemorrhage.

Rupture of the Uterus.—Of the three principal types of rupture of the uterus indicated in Table I, there is little difference of opinion concerning the necessity of hysterectomy in the treatment of spontaneous rupture of the uterus or of traumatic rupture such as occasionally occurs during the performance of version or application of forceps. Such treatment of course presupposes sufficient preparation of the patient to withstand the operative procedure.

Prior to the existence of adequate blood banks to replenish sufficiently depleted reservoirs, the mortality of spontaneous rupture of the uterus was high, and even at present it remains a calamitous emergency. We have been unable to save any babies and have lost two of nine mothers suffering this explosive accident. In each case of death the woman was admitted in desperate circumstances and did not survive an operation performed under much less than optimal circumstances. The seven fortunate individuals who survived the accident had the good fortune to suffer the rupture in the era of multiple transfusions and this preparation, by adequately restoring blood volume, was the controlling factor in their survival.

*Read, by invitation, at a meeting of the New York Obstetrical Society, March 13, 1951.

TABLE I. INDICATIONS FOR PUERPERAL HYSTERECTOMY

Rupture of the uterus
Spontaneous
Traumatic
Postoperative
Abruption of the placenta
Placenta accreta
Placenta previa
Fibromyoma
Infection
Chorionepithelioma
Atony

Close scrutiny of these cases reveals little information useful in anticipating spontaneous rupture except multiparity, for the women in this group had delivered an average of six previous infants prior to their accidents. A minor factor was the neglect of some degree of relative disproportion in two of the women despite their obstetric efficiency indicated by numerous prior deliveries. In each case the infant at the time of rupture was significantly larger than any of those previously delivered.

Three hysterectomies were performed without maternal death because of traumatic rupture occurring during version operations. In each case there was a prolapse of the cord and it is certain that the operator was impelled to proceed with the operation in a determined effort to prevent loss of an infant whose umbilical cord was pulsating more and more slowly, even though the conditions commonly required for version were not completely fulfilled. The error was then compounded by extraction, also in the face of normal contraindications to the operation, i.e., an incompletely dilated cervix. In all three instances the infant was lost, and the mother placed in jeopardy beyond reason.

Our experience with rupture of operative scars has been much more favorable. There have been fourteen ruptures of the uterus through the scars of previous sections or myomectomies without any maternal deaths, and with the loss of five infants. We attribute the good results in this group of women to the routine method of handling such cases whereby they are closely observed, always have blood cross-matched in the blood bank, and are prepared for the possibility of operation whether or not it is determined to allow them trial labor.

Abruption of the Placenta.—Discussion of the treatment of abruption of the placenta at present involves the various methods of treatment of the condition by either conservative or radical measures with little mention of the need of hysterectomy.

While we concur in the opinion that hysterectomy is generally an unnecessary procedure, our experience indicates that a very small number of uteri do suffer sufficient disruption of the myometrium to make contraction sufficient to prevent serious hemorrhage an impossible task. In these very few cases the removal of the uterus does save life.

Four such cases have been reviewed. A 31-year-old gravida xii, para xi, suffered a severe abruption in the course of a rapid and tumultuous labor and after the delivery of her child continued to bleed profusely in spite of oxytocics. The interior of the uterus was clean but dilated and it failed to contract, and hysterectomy was performed promptly followed by an uneventful recovery.

Three women had uteri which behaved in similar fashion after being emptied by cesarean section, and in each case the judgment of the operator led him to remove the uterus. We have generally found that this is only rarely necessary. Usually, by the time the uterine incision is repaired, oxy-

tocics administered, and warm packs placed about the uterus, it will show evidence of sufficient integrity to obviate its removal. We have found this to be true regardless of the appearance of the uterus, which often is initially frightening.

In all four of these cases the myometrium was grossly infiltrated with blood and there was abundant microscopic evidence of rupture of myometrial fibrils. Such muscle disruption we believe to be quite rare.

Placenta Accreta.—This condition, especially in our more recent experience of the past ten years, has been rather rare. It is our belief that the diagnosis is one in which the pathologist alone can give the final opinion, and we have been loathe to make the diagnosis on clinical findings alone unless it is later substantiated by examination of the placenta and the uterus.

We have done three hysterectomies for this condition, two following normal spontaneous delivery in which what appeared to be a retained placenta was found to show no evidence of any cleavage plane between the fetal elements of the placenta and the maternal uterus. In the attempt to delineate a proper plane of cleavage in each of these cases alarming hemorrhage occurred without the plane of cleavage actually developing and the patients were therefore subjected to hysterectomy with the placenta in situ and in each of these cases the microscopic evidence confirmed the diagnosis of placenta accreta. A third case was visualized at the time of cesarean section in which one part of the placenta was firmly ingrown into the myometrium and could not be separated. Upon ablation of this uterus the microscopic appearance of the interspace between the placenta and uterus was found to be typical of that of placenta accreta.

Placenta Previa.—The combination of placenta previa and a fibrotic uterus in relatively old multigravidas has caused us to remove two uteri after delivering the patient by cesarean section.

In each case there was alarming hemorrhage from the placental site after the uterus was emptied and the operator believed it unsafe to close the abdomen in the presence of such bleeding. It is perhaps debatable whether or not these individuals would have bled to death if the uteri had not been removed, but in each case the bleeding was so far in excess of that commonly seen in placenta previa that it is difficult to criticize the operators' judgment. It is worthy of mention that in a few cases of partial previa with vaginal delivery, there was sufficient postpartum hemorrhage to cause us to wish in retrospect that we had done a cesarean-section hysterectomy.

Fibromyoma.—This group represents the indication for which cesarean-hysterectomy is most commonly performed. We have performed 25 such operations without maternal mortality, but will not detail them since in most instances it was done as a convenient method of insuring safe delivery of the infant and also removing the tumors at a single operation.

One patient alone required operation for bleeding, a 36-year-old primigravida with multiple nonobstructing tumors of moderate size. She was allowed vaginal delivery because of her desire for future childbearing, but following delivery bled so profusely in spite of lesser types of treatment that the uterus was removed.

Infection.—We believe the performance of a Porro type of cesarean hysterectomy for infection to be a reprehensible and unnecessary destruction of a woman's childbearing potentiality. The experience of our own and other clinics with various types of extraperitoneal procedures and the excellent results reported by some clinics that use neither the Porro nor the extraperitoneal techniques for infected or potentially infected cases of dystocia, but rely entirely on low cervical cesarean section with the additional protection of antibiotic and chemotherapeutic drugs, would appear to us to indi-

cate that cesarean hysterectomy done for infection as a primary indication is an archaic operation.

Atony.—Table II indicates the pertinent data of the group of cases which has prompted us to undertake this review.

TABLE II. UTERINE ATONY

PATIENT	1	2	3	4	5	6	7
Gravida	4	2	1	1	1	1	5
Age (years)	40	18	27	24	29	24	39
Labor (hours)	6	4	17	11	33	6	9
Spontaneous delivery, low forceps	x	x	x	x			
Low forceps					x	x	
Midforceps rotation							x
Oxytocic administered	x	x	x	x	x	x	x
Cervix inspected	x	x	x	x	x		
Uterus explored	x	x	x	x	x		
Uterus packed		x	x			x	x
Cervix sutured			x				
Curettage						x	x
Hysterectomy	x	x	x	x	x	x	x
Hours post partum	2	2	5	4	15		
Days post partum						14	7

The first patient did not have excessive hemorrhage, the blood loss being less than 1,000 c.c. Operation was performed because of continued bleeding in the presence of what was considered to be a fibrotic noncontractile uterus. Her postoperative course was uneventful.

The second patient had the indicated procedures performed without avail and lost 2,100 c.c. of blood in the two hours between delivery and operation. She received 2,000 c.c. of blood and 1,500 c.c. of plasma by the time the operation was completed. Her postoperative course was uneventful.

The third patient had the indicated procedures performed and bled over 1,000 c.c. in spite of them, with no evidence of abatement of the hemorrhage. Estimated blood loss was replaced prior to and during the operation, and her postoperative course was uneventful.

The fourth patient had the indicated procedures employed and lost over 2,000 c.c. of blood prior to operation. At the time of uterine exploration a small piece of succenturiate placenta was removed but without effect on the nonresponsive relaxation of the uterus. She received 3,000 c.c. of blood and 500 c.c. of plasma and had an uneventful convalescence. The continuance of hemorrhage after removal of a small piece of placenta would indicate that the presence of one cause of bleeding may not exclude others in the same patient.

The fifth patient had an uneventful course until about 3 hours following delivery. She then began to bleed profusely but intermittently. She was in a postpartum room and was treated conservatively with Ergotrate, Pitocin, transfusions, and massage until her condition 15 hours postpartum showed no evidence of amelioration. Exploration of the uterus secured a small cotyledon of placenta. The uterus, however, remained atonic and continued to bleed. Hysterectomy was performed under perhaps less than optimal conditions, the patient having lost about 4,000 c.c. of blood. Prior to, during, and after operation, she received 8,250 c.c. of blood. Her postoperative course was stormy, complicated by a wound dehiscence on the sixth postoperative day, and she had a morbid febrile reaction for 18 days, eventually being discharged on the twenty-third postoperative day. More prompt exploration of this uterus might have obviated operation.

The sixth patient was apparently well without complications until the eighth postpartum day when a gush of bright red blood occurred. This type of bleeding occurred intermittently until the thirteenth day when she was subjected to a curettage without the recovery of any

tissue from the uterus. The uterus at this time was packed. The next day the pack was removed and she continued to bleed very freely. The uterus was again explored both digitally and with a curette without any tissue being obtained, but the bleeding increased at an alarming rate to a total of an estimated 1,850 c.c. blood loss. After hysterectomy her postoperative course was satisfactory. She received 2,500 c.c. of blood.

The last patient of this group did not bleed at the time of delivery but developed a febrile puerperium which subsided by the sixth day under intensive sulfanilamide and antibiotic therapy. She then began bleeding intermittently in alarming amounts. Oxytocics and transfusions were of no avail in stanching the flow of blood, so she was subjected to a curettage, and the uterus packed. She bled excessively through the pack and the uterus was therefore removed. Her postoperative course was complicated by a mild thrombophlebitis but with eventual recovery. The blood loss was more than 2,000 c.c. She received 2,000 c.c. of blood.

In all of these patients postpartum blood studies failed to demonstrate any evidence of the blood dyscrasias, nor did their histories reviewed in retrospect indicate any tendencies to substantiate such a diagnosis.

Since the advent of the availability of adequate blood for transfusion purposes and the protection afforded patients against infection by chemotherapy and antibiotic drugs and perhaps also because of the rather infrequent occurrence of the condition, there have been few studies of the pathology presented in uterine atony. In our experience the examination of these uteri shows an excessive amount of hyalinization of the myofibrils, dilatation of the vessels within the uterine wall, particularly the venous channels, with usually moderate thickening of the vascular walls. The general picture is consistent with that of a rather prolonged degenerative process which our pathologist feels can best be termed "chronic metropathy." The same appearance is not uncommon in uteri removed at cesarean section for fibroids, and might be likened to a premature senile change within the uterus.

Contrary to some reports we have not found the picture presented in the uteri removed for atony consistent with the findings of those uteri removed because of abruptio. There is in general little infiltration of blood and there is little if any actual destruction or breakdown of the myofibrils themselves.

Finally, we have noted a small, rather bizarre group of medical curiosities, the salient feature of each consisting of evidence of hemorrhagic shock post partum without any external evidence of bleeding. Laparotomy revealed in one instance a ruptured venous aneurysm in the broad ligament; in another a rupture of a vein traversing a small fibroid; in a third a tiny fibroid which was avulsed and caused hemorrhage from the pedicle. It is our belief that these are all rare conditions and impossible of accurate diagnosis, but the very presence of hemorrhagic shock should cause the institution of vigorous antishock therapy and exploratory laparotomy as soon as the patient's condition permits. In two of the cases cited hysterectomy was performed, and in the other one venous ligation sufficed.

Comment

This series of cases has been presented to indicate the necessity of considering hysterectomy as a possible final resort in any case of postpartum hemorrhage.

Such hemorrhage remains the principal killer of young women during parturition and although hysterectomy is a final and undesirable method of treatment, it is obvious that it is possible in reviewing any series of deaths from postpartum hemorrhage to say that if at such and such time in the patient's course she had been subjected to hysterectomy, her life would have

been saved. We feel that too often hysterectomy is not considered soon enough in the treatment of postpartum hemorrhage and is finally used in desperation when the patient's condition is too critical for her to withstand the operation.

If at the onset of serious bleeding, not visible in origin, the cervix is inspected and the uterus explored, the more common causes of bleeding will be eliminated. The elimination of deep anesthesia and narcosis and the exhibition of oxytocic parenterally, together with manual stimulation of the uterus, will overcome most instances of bleeding due to atony. During all this time blood must be available and must be used in sufficient quantity. If these measures fail we feel there should be no hesitation in employing hysterectomy as a lifesaving measure. Too much time spent in hopeful waiting, in packing an unresponsive uterus, in employing Spanish windlasses, ligation of the cervical branches of the uterine artery, or even of the uterine artery itself, unless done pending an operation already decided upon, are wasteful of the time so necessary to prevent disaster to the patient. We believe that the only treatment of postpartum hemorrhage that is of any avail short of actually definitive measures is blood in adequate amounts.

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Discussion

DR. R. GORDON DOUGLAS.—I am more or less in complete agreement with what Dr. Cosgrove has stated concerning the value of this operation in the control of postpartum hemorrhage. When uncontrollable bleeding occurs the decision to do a hysterectomy should be reached and the operation carried out before the patient is in complete collapse. Too often one hears of a patient without discernible pulse or blood pressure when the operation is first seriously considered. The indication is encountered quite infrequently but on such occasions it must be considered as a lifesaving procedure. Undoubtedly some patients who recover from a massive hemorrhage are subjected to more than a justifiable risk and might better have been subjected to hysterectomy.

Dr. Cosgrove referred to a fibrotic condition in such uteri when examined pathologically. One might ask then, why does this type of uterus function so well during labor and then in turn respond so poorly post partum?

DR. JOSHUA W. DAVIES.—The removal of the uterus for intractable hemorrhage in a young woman with no other children is a very serious problem. It has occurred to me that the uterine vessels might be ligated to control the bleeding. Then, as in varicose veins, which, when merely ligated, can be expected to recanalize, uterine circulation may be re-established.

DR. E. E. BUNZEL.—I noted in the first six cases, packing of the uterus had been done in three; and one was not done until some days after. The seventh I think also was packed following curettage so that there was a total of four uteri packed but two of them very late. I believe in instituting uterine tamponade for bleeding early following delivery of

the placenta and not waiting until the patient is exsanguinated but rather while the patient is still in good condition. I think the method of tamponade is also a very important factor. The late Dr. Caldwell used to teach his students to pack the uterus by using a lady's stocking, being sure to get the first part of the packing up to the toe. In other words, the entire uterine cavity must be tightly and firmly packed and not just the lower uterine segment, cervix, and vagina. Of course, we have seen cases where even following tamponade of the uterus done under these circumstances, there has been continued bleeding and we have seen cases where hysterectomy has subsequently been done. There is another thing to be considered in looking at the sixth and seventh cases where bleeding was late in occurring. I was wondering if by any chance they might have been in those days before we knew anything about the Rh factor and they might have been Rh negative. There have been some cases where there has been late uterine bleeding and the patients have had transfusions and curettage and later on it was found to have been with incompatible blood. I well remember at least one case where that was done with eventual recovery.

DR. MELVIN L. STONE.—I would like to ask whether fibrinogen determinations and clot retraction studies were made in these reported cases to determine whether or not hemorrhages could be explained on the basis of a blood dyscrasia?

DR. STANLEY C. HALL.—In the hospital with which I am associated, there is an operating room for cesarean sections and hysterectomies in the delivery room suite. Instruments are ready for use within fifteen to twenty minutes in emergency cases. This set up, along with the availability of blood for transfusions, I believe, has saved several babies and mothers during the last year in our hospital where we deliver about 2,600 babies a year. Within the last month there have been two such cases:

1. Abruptio placentae with patient in a marked shock condition. An immediate hysterectomy, with 2,000 c.c. of blood, the first blood being given under pressure, saved this patient's life.

2. Ruptured uterus and marked shock. Because of the extent of the rupture and infiltration of blood in the broad ligament an immediate hysterectomy was done with the saving of the mother's life. It should be the aim of every obstetrical department to be so organized that a cesarean section or hysterectomy can be done in emergency cases, on short notice, within twenty to thirty minutes.

DR. COSGROVE (Closing).—In reply to Dr. Douglas, I was unsuccessful in finding out why these uteri bled. The findings are only negative. They are neither etiological nor pathognomonic. I think it is quite certain there is no anatomical lesion that causes abnormal lack of response of these uteri.

Dr. Davis, in regard to ligation of uterine arteries I have either done or helped ligate the uterine arteries on both sides and I don't think it stops the uterus from bleeding. If the uterus is going to bleed, there is quite enough blood from the ovarian arteries to allow the patient to bleed to death. From above at the time of cesarean section you can tie both uterine arteries off without causing any particular trouble to the uterus. There have been cases in which the uterine artery ruptured when we had to do that, and there have been several cases where they were both tied off without any apparent trouble so far as the woman's future childbearing is concerned.

Dr. Hall, I quite agree. Our whole philosophy of treating pregnant women is that we are prepared at any time to do a cesarean section or a hysterectomy if necessary. We believe that once a cesarean section by no means necessarily means a subsequent cesarean section. We are quite willing to give certain individuals who have had a cesarean section a subsequent trial labor if it appears they will deliver vaginally and the whole philosophy of such management is based on having an operating room ready.

Dr. Stone, one of these cases, the last one, did get fibrinogen. For the rest of them, blood studies were not done until they were obviously getting better and we didn't expect to

find anything abnormal. We don't know if there was anything abnormal at the time of serious bleeding but in view of the necessity for doing major surgery, we just didn't get around to doing laboratory work that might have been interesting to have later on.

Dr. Madden and Dr. Bunzel spoke about packing. I have never packed a uterus in my life that I recall and I don't intend to and the general attitude of the clinic is not to pack uteri. I don't know how these two particular uteri got packed. It is not the usual way we handle cases of postpartum hemorrhage. If you are going to do any actual massage or have anything in the uterus, we feel quite certain the best thing is your own fist with the other hand outside the abdomen and in that way the uterus may be massaged, and if it expands you can follow it with your fist. Perhaps if continuously packed, it might stop but when one considers the size of a term uterus it would take a lot of gauze to fill it up. So far as the Rh factor is concerned, there was nothing unusual about the Rh factor in those cases in which it was known.

About Dr. Smith's question on ruptured uteri: Frankly, there were 3 ruptured uteri not subjected to hysterectomy. As a matter of fact, one patient accounted for two of the ruptures, the first with her second pregnancy. We extracted the baby through the rupture of the wound and in the third pregnancy it ruptured again, and the third time we took the uterus out. Ordinary rupture, with reasonably well-healed previously sectioned scar, is quite possible to repair without having to take the uterus out. We don't believe this to be true in spontaneous rupture.

AN ANALYSIS OF 45 FACE PRESENTATIONS*

A. Charles Posner, M.D., F.A.C.S., and Sidney Cohn, M.D., New York, N. Y.

(From the Bronx Hospital)

THE incidence of face presentation is very small. Most textbooks state that its incidence ranges from 1 in 200 to 1 in 300. Hellman and associates recently found the incidence to be 1 in 356. On the other hand, other authors have reported incidences ranging between 1 in 529 and 1 in 576.

This paper deals with all face presentations delivered at the Bronx Hospital from Jan. 1, 1936, through June 30, 1950. During that time there have been forty-five such cases in 36,021 deliveries, an incidence of 1 in 800, or 0.125 per cent.

It is the purpose of this paper to analyze these cases and to discuss various aspects of this uncommon presentation.

Material

The forty-five women in this series ranged in age from 20 to 40, with an average age of 28.8 years. Twenty-seven (60 per cent) were between 20 and 30 years of age, ten (22.2 per cent) were between 31 and 35, and eight were between 36 and 40 years of age.

Twenty-one of the patients were nulliparous, and twenty-four were multiparous. The highest parity in this series was five.

Etiological Factors

The main causative factors in face presentation have been discussed in other reports. In thirty-five of the forty-five cases comprising this series, one or more contributing factors were found. The most common of these was some type of cord dystocia, either a short cord or cord around the neck of the fetus. This was present in fifteen of the cases. Other frequently present factors were contracted pelvis, immature or premature infants, fetal monstrosities, and large babies. The actual incidence of these predisposing conditions is shown in Table I.

Table I. Etiological Factors

ETIOLOGICAL FACTORS	NO. OF CASES
Cord dystocia:	
a. Around neck	9
b. Short cord	6
Contracted pelvis	9
Monstrosities	7
Large baby:	
8½ to 10 pounds	6
10 pounds and over	1
Prematurity	6
Hydramnios	1
No apparent cause	10

*Read, by invitation, at a meeting of the New York Obstetrical Society, March 13, 1951.

Mechanism of Labor

It should be noted that the criterion for engagement of vertex presentations, namely, that the biparietal diameter has passed through the brim of the pelvis, cannot be applied for face presentations, as the distance from the parietal eminences to the face is greater than to the occiput. Thus the face must descend considerably below the level of the ischial spines before we may conclude that the trachelobregmatic and biparietal diameters have passed the superior strait.

The mechanism of anterior chin presentations is similar to that of vertex presentations with the chin instead of the occiput as the point of reference.

Three possible abnormalities in the mechanism were first described by Hirst:

1. Internal rotation in the transverse or posterior positions may be delayed due to mechanical difficulty, as the chin must descend to a lower level before meeting the necessary soft tissue resistance. The fetal neck must stretch since its length is normally less than one-half the depth of the posterior pelvis.
2. Delivery is mechanically impossible with posterior rotation of the chin to the hollow of the sacrum.
3. Arms displaced into the cavity of the extended back of the fetus greatly impede its progress.

Molding occurs with the usual shortening of the engaging diameter, here the trachelobregmatic, with compensatory lengthening of the directional diameter, the occipitofrontal. The caput succedaneum occurs over most of the face, and is pronounced in both anterior and posterior mentum presentations.

Position

The incidence of the various positions is shown in Table II. We have found that 44.4 per cent of the cases engaged in the right oblique, 40 per cent engaged in the left oblique, and 11 per cent presented transversely. In the remainder of the cases the exact position was not stated. Our figures are similar to those of both Rudolph and Hellman who found an almost equal distribution between right mentum anterior and left mentum posterior on one hand, and right mentum posterior and left mentum anterior on the other.

Clinical Course

If one considers "at term" to denote the expected date of confinement plus or minus two weeks, then twenty-eight (62.2 per cent) of our patients fall into this category. Eight patients delivered two to six weeks before their due dates, and three patients delivered previable babies. An additional four women were delivered two to four weeks after their expected time. In two cases, the expected date of confinement was unknown. Although the number of cases is small, we cannot help but detect a tendency toward premature labor.

TABLE II. POSITION OF FETUS AT TIME OF DIAGNOSIS

POSITION	NO. OF CASES
Left mentum anterior	12
Left mentum transverse	2
Left mentum posterior	5
Right mentum anterior	13
Right mentum transverse	3
Right mentum posterior	8
"Face"	1
"Mentum posterior"	1

It is generally believed that the first stage of labor is prolonged with face presentations. In determining the length of the stages in this series, we have eliminated (1) those cases in which a premature or macerated fetus was delivered; (2) those cases in which a cesarean section was done; (3) those cases in which the original position was not stated. Nonmacerated stillborn infants weighing over 5 pounds were included. In all, thirteen cases were eliminated.

In the remaining thirty-two cases, the average length of the first stage in nulliparous women delivering from the anterior or transverse positions was twenty hours. For multiparous patients, it was twelve hours, thirty-five minutes. These figures approximate the average length of the first stage in vertex presentations. This is contrary to former beliefs, and yet is more in accord with the findings of Tucker.

Tucker and her co-authors believe the second stage to be slightly prolonged. Our findings would tend to suport that idea, for in five primiparous women delivering from the anterior or transverse chin positions, the second stage averaged two hours, twelve minutes, and in twelve multiparous women, it averaged forty-two minutes. While the number of cases is small, it is felt that the frequency with which this prolongation is found is a good indication that such is the rule.

In patients with mentum posterior positions, labor was markedly prolonged, the average length of labor being sixty hours and thirty-nine minutes.

Membranes tend to rupture early in contrast to vertex presentations where they usually rupture at the onset of the second stage. In sixteen cases, the membranes ruptured before or at the onset of labor. In seventeen cases, they ruptured during the first stage, and in two instances they were ruptured artificially during that stage. Excluding these two cases and the one case where the membranes were ruptured at cesarean section, the membranes were found to have ruptured before the end of the first stage in 80 per cent of the cases. Table III shows the incidence of rupture of the membranes in the various stages.

TABLE III. TIME OF RUPTURE OF MEMBRANES

TIME	NO. OF CASES
Before onset of labor	8
At onset of labor	8
First stage, spontaneous	17
First stage, artificial	2
Second stage, spontaneous	4
Second stage, artificial	5
At operation	1

Diagnosis

The diagnosis of a face presentation may be made in four different ways. First, it should be suspected on abdominal examination when the cephalic prominence is palpated on the same side as the dorsum. This, plus a high presenting part, strongly supports the diagnosis of face presentation.

Rectal and vaginal examinations offer the second and third possible methods of diagnosis. Here one encounters a firm, irregular presenting part with depressions and prominences. This finding, after elimination of the possibility of a breech presentation via Leopold's maneuvers, should aid in establishing the diagnosis.

Finally, the diagnosis can be made or confirmed by x-ray examination. Caution must be exercised in accepting the report of the radiologist as final, especially if the films were taken before the onset of labor. These films must be taken during labor, for we have encountered instances where x-rays taken

prior to the onset of labor revealed vertex presentations, and then during labor a face presentation was diagnosed. The converse of this is true. When in doubt we do not hesitate to repeat x-rays during labor.

In Table IV are shown the means and times of the diagnosis in this series.

TABLE IV. TIME AND MEANS OF DIAGNOSIS

MEANS	BEFORE ONSET OF LABOR	FIRST STAGE	SECOND STAGE	AT DELIVERY	PRESENTING PART AT VULVA
Suspected abdominally		3			
Rectal	1	7	1		
Vaginal		4	5	20	3
X-ray:					
Diagnosis	1				
Confirmation		3			
Total time of suspicion	2	14	6	20	3

Management and Results

The management and results in this series are shown in Table V. Twenty-nine (64.44 per cent) patients delivered spontaneously. In this group there were 11 fetal deaths, an over-all mortality of 38.0 per cent. However, 6 were monsters and one was immature, leaving a corrected fetal mortality for normal babies of 13.8 per cent. In 2 cases the fetal heart tones were not heard on admission; in one, the fetal heart tones were lost during the first stage; and in the last, although the fetal heart was heard up to the time of delivery, a stillborn infant with two loops of cord around the neck was delivered.

TABLE V. MANAGEMENT AND RESULTS IN 45 FACE PRESENTATIONS

	FULL TERM			PREMATURE				
MANAGEMENT	LIVE BIRTHS	STILLBIRTHS OR NEONATAL DEATHS	MONSTROSITY	LIVE BIRTHS	STILLBIRTHS OR NEONATAL DEATHS	MONSTROSITY	TOTAL BIRTHS	MATERNAL DEATHS
Spontaneous delivery	17	4	3	1	1	3	29	
Version	2	1	1		1		5	1
Cesarean	6						6	
Kielland	1						1	
Dewees		1					1	
Low forceps	2				1		3	

Three patients were delivered by low forceps. There was one fetal death in this group, of an immature infant weighing one pound, 13 ounces.

One patient was delivered with Kielland forceps. The cervix had been fully dilated for more than two hours. The position was right mentum transverse.

One patient was delivered by Dewees midforceps. She was a primigravida with a forty-hour first stage. Six hours before the cervix became fully dilated, the fetal heart tones disappeared. After two hours of full dilatation, a Dewees midforceps extraction of a stillborn infant was done. The Dewees forceps is a powerful forceps, and it is felt that it, with its French lock, is too powerful to be applied to a face because it may prove injurious to the facial bones. Therefore, in face presentations, the use of the Dewees forceps should be condemned except where a stillbirth is anticipated, in which case it may serve as an excellent adjuvant in terminating a delivery.

Five patients were delivered by version and extraction. There were 3 stillborn infants, one of whom was a monstrosity, and the other an immature infant. The third stillbirth occurred in a 32-year-old primigravida who had a sixty-four hour labor with a persistent right mentum posterior. Kielland forceps were applied and the chin rotated anteriorly. When descent could not be effected, examination revealed a Bandl's ring which did not respond favorably to deep anesthesia. The patient was given morphine, Adrenalin, and intravenous fluids. Six hours later a version and breech extraction were done, and Piper forceps were used for the aftercoming head. The result was a 9-pound stillborn infant. Immediately after delivery the patient went into shock. The uterus was soft and "boggy," and examination revealed tears in the fornix and lower uterine segment. The patient never reacted from the anesthesia and died one hour and twenty minutes later. Postmortem examination revealed a ruptured uterus with intraperitoneal and retroperitoneal hemorrhage. This was the only maternal death in this series. It was an error in judgment and diagnosis. She should have been delivered by cesarean section much earlier. In the remaining two cases, version was done in the first for prolapse of the cord and arm, and in the other, for mentum posterior with fetal distress.

Cesarean section was elected for delivery in 6 patients (13.3 per cent). One of these was a repeat section. In the remaining 5 patients, one or more of the following indications were present: cephalopelvic disproportion, contracted pelvis, mentum posterior, and fetal distress.

Comment

The unusually low incidence of face presentation reported in this series is in sharp contrast to previous reports and textbook statements. We are unable to offer any tenable explanation for this finding. However, it should be pointed out that one contributing etiological factor, namely, the "grande multipara," is becoming an entity of the past, especially in urban populations.

Concerning etiological factors in this condition, the findings in this series approximate those reported by one of us in a previous report. They are also in accord with those of Rudolph who found some degree of disproportion, manifested by either an abnormal pelvis or a large baby, in almost 50 per cent of his cases. In this series we have found disproportion to be present in 16 of the 35 cases (45.8 per cent) in which an etiological factor could be demonstrated. Equally as common as cephalopelvic disproportion was the presence of cord dystocia, i.e., a short cord or a loop of cord around the neck of the fetus. Such a condition was present in 15 cases. The frequency of this condition suggests its importance in the causation of face presentation, and parallels that of cephalopelvic disproportion.

Our findings do not parallel those of Tucker and associates, who found the most common factors to be occiput posterior and multiparity. We are unable to disregard all the other factors enumerated previously. That multiparity is a factor in causing face presentation is generally accepted, but the role of occiput posterior position, per se, predisposing to face presentation is dubious. There must be other factors involved, some known, others unknown, which play a part, for if that were not the case, then a greater number of cases of occiput posterior whose initial incidence according to Davis is up to 30 per cent of all vertex presentations, would convert to mentum anterior.

In this series there were 16 stillbirth and neonatal deaths, an over-all mortality of 35.5 per cent. However, elimination of all abnormal infants leaves a gross mortality of nine in thirty-eight, or 24.7 per cent for normal infants.

Further scrutiny is warranted in determining the fetal salvage if we are to determine the true mortality rate. Certainly, premature infants, macerated stillborns, and those cases in which the fetal heart tones are not heard on admission, cannot be counted against the obstetrician. These considerations leave us with a corrected fetal mortality of 4 in 33, or 12.1 per cent.

We believe in the old dictum, "If a face is making progress, leave it alone." However, there is one type that must not be left alone, and that is the mentum posterior. In the present series there were 14 such cases. In 10 of these, live babies were obtained: 6 by cesarean section, one by version and extraction, and 3 by spontaneous delivery after rotation. The remaining 4 cases resulted in stillbirths. Two infants were monstrosities, one delivering spontaneously, and the other by version and extraction. Of the other 2, one delivered spontaneously, and the other had a difficult operative delivery. So, only 5 of the 14 patients with mentum posterior presentation delivered spontaneously, and of these infants, one was stillborn, and one was a monster. The labor with mentum posterior is long and hard, and usually terminates with operative interference which is hazardous to the baby. In the 5 patients who delivered infants of normal size via the vaginal route, the average length of labor was sixty hours, forty-nine minutes. Cesarean section for lack of progress in mentum posterior positions must be kept in mind.

Summary and Conclusions

1. A review of forty-five consecutive face presentations in 36,021 deliveries at the Bronx Hospital has been presented.

2. The incidence of this presentation is much less than has ever been reported.

3. The etiological factors have been enumerated, the most common being cord dystocia and contracted pelvis.

4. There is almost equal distribution between presentations lying in the right and left oblique diameters.

5. In face presentations there is a tendency toward premature labor.

6. In 40 per cent of the cases the membranes ruptured before or at the onset of labor, and in an additional 40 per cent they ruptured before the end of the first stage of labor.

7. A plea is made for x-ray studies to aid in, or confirm, the diagnosis of face presentation. Repeated x-rays may be necessary during labor.

8. Cesarean section for lack of progress in mentum posterior positions must be considered.

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Discussion

DR. CLAUDE E. HEATON.—At Bellevue Hospital since 1933 we have had an incidence of one face presentation to 487 deliveries. Parity did not seem to play a role. X-ray studies showed the pelvis to be ample in the majority of cases. We were surprised to find that over one-half of the cases with the mentum posterior delivered spontaneously. We had a gross fetal mortality of 18 per cent and a corrected fetal mortality of 10.4 per cent. In the management of face presentation our results with version were not good. We agree with Dr. Posner that cesarean section is the best treatment in the presence of pelvic contraction. In patients with an adequate pelvis failure of the chin to rotate anteriorly can be treated by delivery with the Kielland forceps. In two instances Barton forceps were used successfully.

DR. EDW. H. DENNEN.—The main interest in Dr. Posner's paper on face presentation seems to be centered on the operative management of delivery. For many years the procedures taught and accepted as standard have been flexion and manual rotation followed by forceps, or, failing in these, version. With these methods the infant mortality has been high, the highest of any presentation, except possibly that of breech.

But if we consider the more modern concepts in the management of face presentation, we find that the mortality is less if we abandon some of the more difficult procedures, substituting the advantages of the newer special types of forceps or more frequent use of cesarean section.

The important factors to be considered before deciding upon an operative delivery by vagina are: the question of disproportion; the condition of the cervix; and the type and length of labor. In the average case, with a short labor, clinical and x-ray evidence of no disproportion, the cervix fully dilated and the chin anterior in the lower half of the pelvis a forceps delivery as such, without manual manipulation, should not be particularly difficult. The instrument to be used should be a Simpson type, as its long tapering cephalic curve tends to fit the molding of the face. It should have some form of axis-traction attachment in order best to preserve extension until the chin is delivered. Instrumental axis traction automatically directs the force in the axis of the pelvis, thereby diminishing the effort necessary for delivery.

Dr. Posner condemns the Dewees forceps because of injury to the facial bone. I have not had that experience and I wonder if his opinion is based on enough cases having this complication. The Dewees is an excellent instrument particularly for its fixed axis traction attached to the handle. It must be kept in mind that the Dewees is a powerful instrument and traction should be applied gradually to determine the amount of force necessary for the normal advance of the head. It is not an uncommon experience for operators, after failure with a non-axis-traction forceps to change to the Dewees and immediately apply the same amount of force which was unsuccessful with the first instrument. The result usually is a rapid advance of the fetal head accompanied by injuries to both the mother and baby.

For anterior chins in the upper pelvis the Tarnier can be used in the occasional case because of its long shanks and excellent axis traction. It has the best type of movable axis traction of any instrument. For years it was used in occiput presentations in the upper pelvis when cesarean was considered too dangerous. It has since fallen into disrepute because of its narrow cephalic curve which caused so much intracranial injury. The undesirable brow-mastoid application was a common result due to the difficulty in obtaining a true cephalic application on heads not in the anterior position. This risk was accepted because it was safer for the mother.

When the chin is in the transverse or posterior position, I have felt for some time that the simplest method of delivery in most cases, and the one offering the best results, is with the use of the Kielland forceps. A single accurate application without displacement of the head followed by rotation of the chin to anterior can be accomplished with one maneuver. If the chin is directly posterior the method used is the upside down direct application of the Kiellands to the sides of the face. This is followed by anterior rotation and traction.

The main exception, in fact the contraindication to the use of the Kielland, forceps is a flat pelvis or a deformed sacrum requiring the mechanism of labor for a flat pelvis. Here, with the chin in transverse arrest the instrument of choice is the Barton forceps. It is the only available instrument that can be used safely in such a case. Its special type of construction permits traction and descent of the head in the required transverse position to low pelvis before rotation to the anterior position.

DR. FRANK P. LIGHT.—As I recall, Dr. Louis M. Hellman reported from the Johns Hopkins Hospital an incidence of contracted pelvis in about 50 per cent of their cases with face presentation. In our series at the Long Island College Hospital, there were very few contracted pelvis. This, as I gather from Heaton's remarks, is the experience at Bellevue. In Dr. Posner's series of 46, there were 9 contracted pelves, roughly 20 per cent. Hence it would appear that, in this area, contracted pelvis plays a small part in the etiology of face presentation. In our material, the most common causative factor is marked deviation of the uterus from its normal axis.

Apparently we are all in accord that anterior face presentation with a normal pelvis offers no problem. Spontaneous delivery can usually be anticipated.

It is most interesting to me that Dr. Posner did not even mention, nor did Dr. Heaton, the time-honored method of flexion of the posterior face. It is used routinely in our clinic, with success in more than 75 per cent of our cases. We do not allow posterior face to continue as such once the membranes have ruptured. Immediately after rupture of the membranes, the posterior face is converted or flexed to an anterior occiput presentation. If this cannot be accomplished, we rotate it to an anterior face. Failing either of these maneuvers, which is rare, we formerly resorted to version, but now prefer cesarean section.

We have a rather large series of face cases, a report of which is now in preparation by Dr. M. V. Armstrong. The series is unique because of the high incidence of success with flexion or conversion. We feel that our success with the maneuver is due to the fact that we employ it immediately after rupture of the membranes.

DR. J. J. MADDEN.—In face presentations, I believe we must make a distinction between primiparas and multiparas.

In the multiparous patient, face presentation does not offer great difficulties. With an anterior chin, most will deliver spontaneously or with some aid as flexion and forceps extraction. The posterior chin cases can usually be handled by flexion-rotation and forceps extraction or by version and extraction.

In the primiparous patient, if the condition is discovered early, I believe the best treatment is cesarian section in all cases, regardless of position, particularly if one is desirous of a low fetal mortality.

CRITERIA OF INLET CONTRACTION. WHAT IS THEIR VALUE?

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(From the Department of Obstetrics, University of Maryland Medical School)

PRIOR to the introduction of chemotherapy and antibiotics, it was the feeling and teaching that the safest time to do a cesarean section was before the onset of labor. The risk to the mother increased with the length of labor and rose sharply with the rupture of the membranes. Therefore, it was most important to evaluate the pelvis and to elect abdominal delivery on that group in which it fell below an arbitrarily chosen limit. This was usually on the basis of the estimated true conjugate as determined by manual measurement of the oblique conjugate. Obstetricians spoke very glibly of absolute indications, broadened absolute, and relative indications. A great deal of dependence was placed upon this diagonal conjugate and while not infrequently a small measurement meant elective section, a large one prohibited it, even in the face of evident disproportion.

This measurement has been evaluated in a previous communication by the author[1] and has been proved to be so inaccurate as to be rather undependable. It was hoped that with the more accurate means of pelvic mensuration more consistent predictions could be given. In order to reach this goal there have been various methods evolved to predict more accurately the outcome of labor and even to make the prognosis for elective cesarean section. Some of these "yardsticks" have been the: (1) obstetrical conjugate, (2) Mengert's[2] areas, (3) Allen's[3] areas, (4) Moir's[4] approach, (5) Weinberg and Scadron's[5] sum, etc. All appear to have been of value in the hands of those originating them. Many obstetricians, using these yardsticks, have assumed that they are infallible and have submitted their primigravidas with vertex presentations to prelabor cesarean sections in a Mengert's area of 110 or Allen's area of 87 sq. cm., or an obstetrical conjugate of 9.0 cm., or Weinberg and Scadron's sum of 21.4 cm., etc. The question arises: "Is this confidence justified?" With this idea in mind it was thought worth while to endeavor to find out: (1) if elective cesarean section is ever justified in a primigravida with a vertex presentation with the use of the recommended criteria, and (2) to consider their dependability when other obstetricians use them.

Material and Methods

During the years July 1, 1947, to July 1, 1950, 1,169 x-ray pelvimetries were done at the University Hospital, Baltimore, Maryland. These were made with the Steele-Javert technique of pelvimetry, which in our hands has a maximum of 3 per cent error. These x-rays were all taken on suspect pelves.

They were all read by one observer and the results of delivery in these pelves were classified according to Mengert's areas and drawing, Allen's areas, Moir's method of determining inlet obstruction, Weinberg and Scadron's sum of the obstetrical conjugate and the transverse diameter, and by single diameters and combination of diameters. Difficult deliveries are defined as follows: (1) The biparietal diameter of the fetal head has not passed the inlet after a well-defined trial of labor and cesarean section is done, and (2) vaginal delivery has been accomplished but the babies have had intracranial injury. All cases of elective cesarean section have been omitted as well as all sections for uterine inertia. All other deliveries were considered easy or normal.

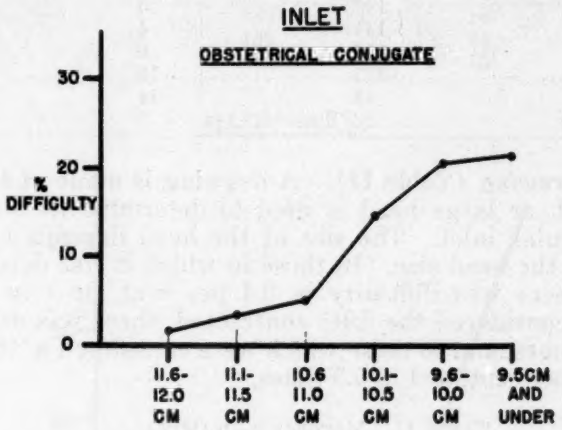

Fig. 1.

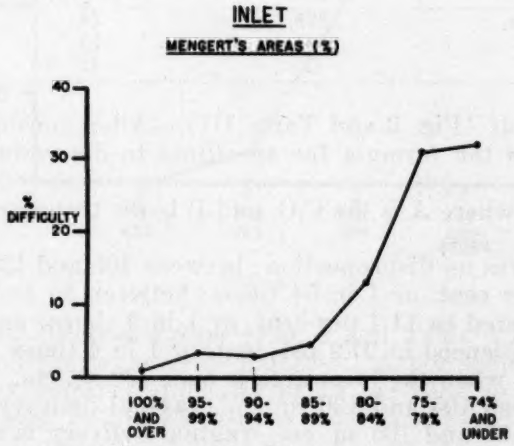

Fig. 2.

Results

1. Obstetrical Conjugate Alone (Fig. 1).—An obstetrical conjugate of 10.0 cm. is considered border line by most authors. Above 10.0 cm. there was difficulty in 4.2 per cent or 1 in 25 cases, while below the border line, there was difficulty in only 20 per cent, or 1 in 5 cases. Note that there was inlet obstruction even when the C.O. was 11.6 cm. or over. In these patients one of two factors was present, either an excessive-sized baby or a contracted transverse diameter.

2. Mengert's Areas (Fig. 2, Table I).—This area is obtained by multiplying the C.O. and the transverse diameter. One hundred per cent of normal is 145 sq. cm. Border line is considered to be 85 per cent of normal, or 123.25 sq. cm. Above border line there was difficulty in 2.3 per cent of cases, or 1 in 43 patients, and below border line there was difficulty in 19.2 per cent of cases, or 1 of every 5 patients.

TABLE I. INLET, MENGERT'S AREAS

AREAS	TOTAL NUMBER OF CASES	NUMBER OF DIFFICULT	% DIFFICULT
100% and over	349	3	0.86
95-99%	147	5	3.4
90-94%	141	4	2.8
85-89%	137	6	4.4
80-84%	123	16	13.0
75-79%	48	14	31.2
74% and under	22	7	31.8

3. Mengert's Drawing (Table II).—A drawing is made of the inlet and a small, medium-sized, or large head is used to determine its ability to adapt itself to this particular inlet. The size of the head depends on clinical and x-ray evaluation of the head size. In those in which it was decided there was no disproportion there was difficulty in 3.4 per cent, or 1 in 30 times. In those in which we considered the inlet contracted, there was difficulty in 27.2 per cent, or 1 in 4 times, and in those which were considered a "toss-up," there was trouble in 18.5 per cent, or 1 in 5.5 times.

TABLE II. MENGERT'S DRAWING

PREDICTION	TOTAL NUMBER OF CASES	NUMBER OF DIFFICULT	% DIFFICULT
No disproportion	828	28	3.4
Borderline	81	15	18.5
Contracted	55	15	27.2

4. Allen's Areas (Fig. 3 and Table III).—Allen considers the inlet to be an ellipse and uses the formula for an ellipse to determine inlet area. This formula is $\frac{\pi \text{ AB}}{4}$, where A is the C.O. and B is the transverse diameter. Over 130 sq. cm. there was no disproportion; between 105 and 129 sq. cm. there was difficulty in 1.8 per cent, or 1 in 54 times; between 85 and 104 sq. cm., difficulty was encountered in 11.4 per cent, or 1 in 9 times; and below 84 sq. cm. difficulty was experienced in 27.2 per cent, or 1 in 4 times. Allen's prognosis is as follows: (1) when the brim area is over 130 sq. cm., vaginal delivery is certain; (2) between 105 and 130 sq. cm., vaginal delivery is reasonably certain; (3) between 85 and 105 sq. cm., vaginal delivery is uncertain; and (4) below 85 sq. cm., vaginal delivery is extremely unlikely. In our experience we can certainly agree with the first two statements.

TABLE III. ALLEN'S INLET

AREA	TOTAL NUMBER OF CASES	NUMBER OF DIFFICULT	% DIFFICULT
130 and over	79	0	0
105-129	487	9	1.8
85-104	378	43	11.4
84 and under	22	6	27.2

5. Moir's Method (Fig. 4 and Table IV).—Moir measures the biparietal diameter of the fetal head antenatally and then correlates it with the C.O. and the average or available transverse diameter. His graph[4] must be used to interpret disproportion. In evaluating this material the way he suggests, we found difficulty in 2 per cent, or 1 in 50 times when no disproportion was suspected, 17.4 per cent, or 1 in 6 times when it was considered border line, and 41.6 per cent, or 1 in 2.4 times when it was deemed a contracted inlet.

TABLE IV. MOIR'S INLET

PREDICTION	TOTAL CASES	NUMBER OF DIFFICULT	% DIFFICULT
No disproportion	789	16	2.0
Borderline	138	24	17.4
Contracted	36	15	41.6

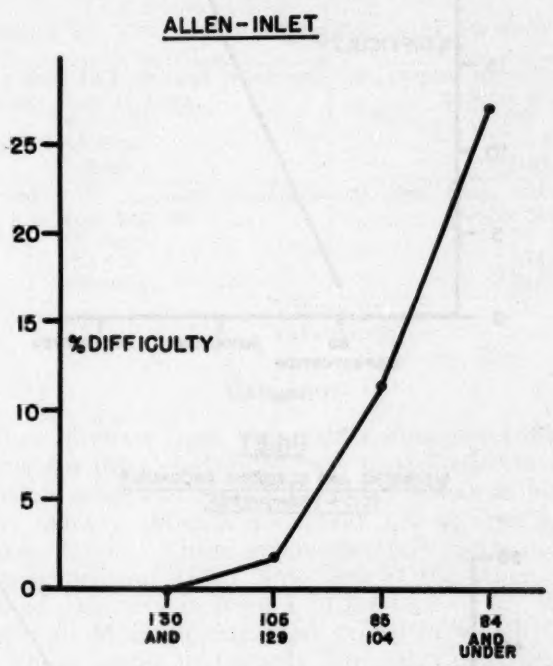

Fig. 3.

6. Weinberg and Scadron's Sum (Fig. 5 and Table V).—Their sum consists of the C.O. and the transverse diameter. A borderline sum is 22.0 cm. Above 22 cm. we experienced difficulty in 2.7 per cent, or 1 in 37 cases and below it in 22.6 per cent, or 1 in 4.4 cases.

TABLE V. INLET, WEINBERG AND SCADRON

SUM	TOTAL NUMBER	NUMBER DIFFICULT	% DIFFICULT
20.0 and under	2	1	50.0
20.1-21.0	25	9	36.0
21.1-22.0	123	24	19.5
22.1-23.0	217	12	5.5
23.1-24.0	237	7	3.0
24.1-25.0	205	3	1.5
25.1 and over	162	0	0

2. Mengert's Areas (Fig. 2, Table I).—This area is obtained by multiplying the C.O. and the transverse diameter. One hundred per cent of normal is 145 sq. cm. Border line is considered to be 85 per cent of normal, or 123.25 sq. cm. Above border line there was difficulty in 2.3 per cent of cases, or 1 in 43 patients, and below border line there was difficulty in 19.2 per cent of cases, or 1 of every 5 patients.

TABLE I. INLET, MENGERT'S AREAS

AREAS	TOTAL NUMBER OF CASES	NUMBER OF DIFFICULT	% DIFFICULT
100% and over	349	3	0.86
95-99%	147	5	3.4
90-94%	141	4	2.8
85-89%	137	6	4.4
80-84%	123	16	13.0
75-79%	48	14	31.2
74% and under	22	7	31.8

3. Mengert's Drawing (Table II).—A drawing is made of the inlet and a small, medium-sized, or large head is used to determine its ability to adapt itself to this particular inlet. The size of the head depends on clinical and x-ray evaluation of the head size. In those in which it was decided there was no disproportion there was difficulty in 3.4 per cent, or 1 in 30 times. In those in which we considered the inlet contracted, there was difficulty in 27.2 per cent, or 1 in 4 times, and in those which were considered a "toss-up," there was trouble in 18.5 per cent, or 1 in 5.5 times.

TABLE II. MENGERT'S DRAWING

PREDICTION	TOTAL NUMBER OF CASES	NUMBER OF DIFFICULT	% DIFFICULT
No disproportion	828	28	3.4
Borderline	81	15	18.5
Contracted	55	15	27.2

4. Allen's Areas (Fig. 3 and Table III).—Allen considers the inlet to be an ellipse and uses the formula for an ellipse to determine inlet area. This formula is $\frac{\pi AB}{4}$, where A is the C.O. and B is the transverse diameter. Over 130 sq. cm. there was no disproportion; between 105 and 129 sq. cm. there was difficulty in 1.8 per cent, or 1 in 54 times; between 85 and 104 sq. cm., difficulty was encountered in 11.4 per cent, or 1 in 9 times; and below 84 sq. cm. difficulty was experienced in 27.2 per cent, or 1 in 4 times. Allen's prognosis is as follows: (1) when the brim area is over 130 sq. cm., vaginal delivery is certain; (2) between 105 and 130 sq. cm., vaginal delivery is reasonably certain; (3) between 85 and 105 sq. cm., vaginal delivery is uncertain; and (4) below 85 sq. cm., vaginal delivery is extremely unlikely. In our experience we can certainly agree with the first two statements.

TABLE III. ALLEN'S INLET

AREA	TOTAL NUMBER OF CASES	NUMBER OF DIFFICULT	% DIFFICULT
130 and over	79	0	0
105-129	487	9	1.8
85-104	378	43	11.4
84 and under	22	6	27.2

5. Moir's Method (Fig. 4 and Table IV).—Moir measures the biparietal diameter of the fetal head antenatally and then correlates it with the C.O. and the average or available transverse diameter. His graph[4] must be used to interpret disproportion. In evaluating this material the way he suggests, we found difficulty in 2 per cent, or 1 in 50 times when no disproportion was suspected, 17.4 per cent, or 1 in 6 times when it was considered border line, and 41.6 per cent, or 1 in 2.4 times when it was deemed a contracted inlet.

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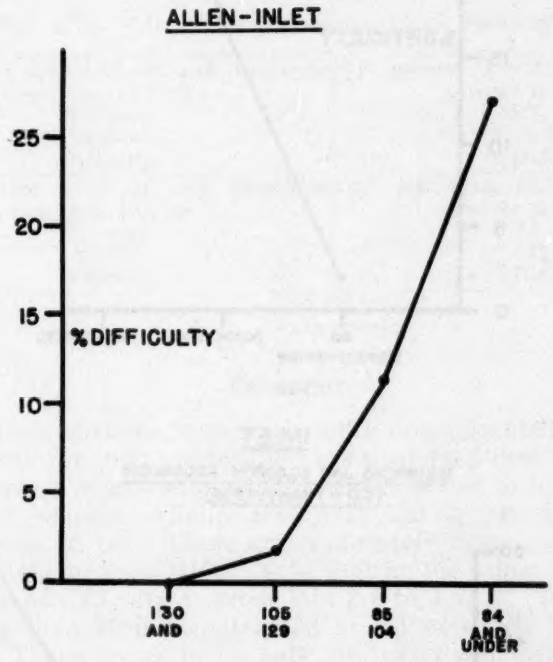

Fig. 3.

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24.1-25.0	205	3	1.5
25.1 and over	162	0	0

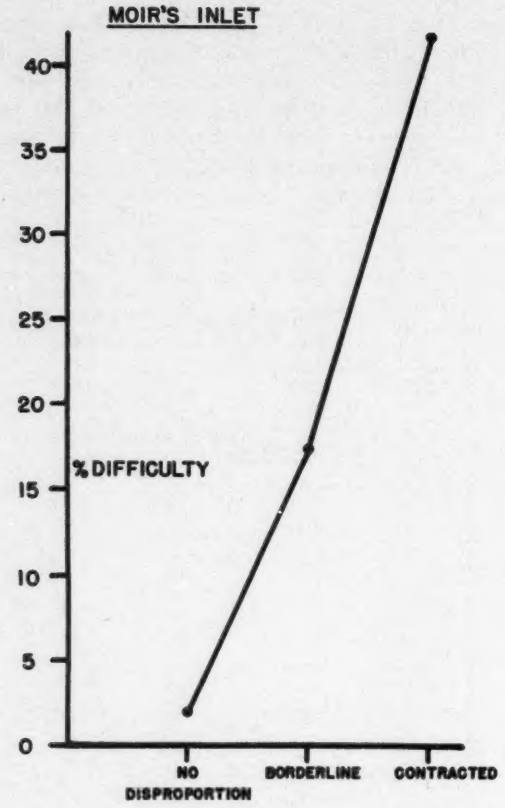
MOIR'S INLET
40
35
30
25
20
% DIFFICULTY
15
10
5
0
NO DISPROPORTION
BORDERLINE
CONTRACTED

Fig. 4.

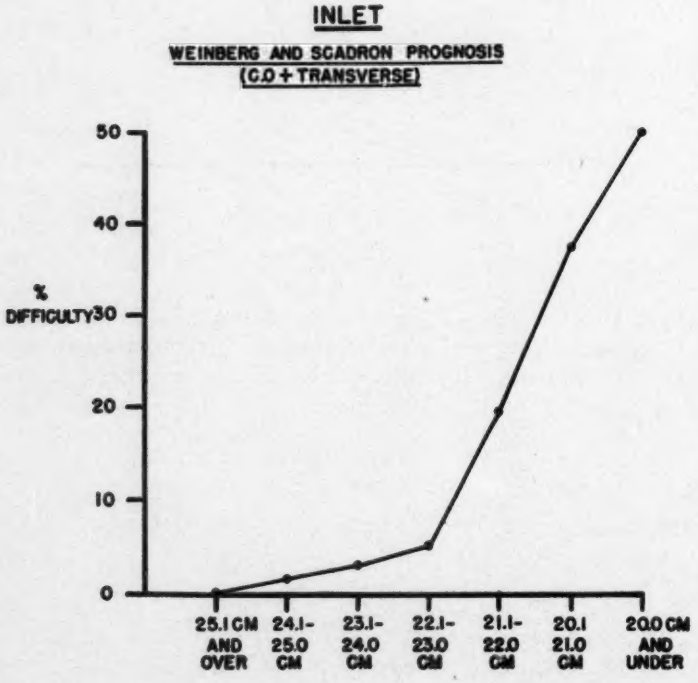
INLET
WEINBERG AND SCADRON PROGNOSIS
(C.D + TRANSVERSE)
50
40
%
DIFFICULTY30
20
10
0
25.1 CM AND OVER
24.1-25.0 CM
23.1-24.0 CM
22.1-23.0 CM
21.1-22.0 CM
20.1 21.0 CM
20.0 CM AND UNDER

Fig. 5.

7. Correlation of C.O. and Transverse Diameter (Table VI).—A scattergram was made with the C.O. and transverse diameter as factors. Table VI is a simplification of this scattergram. All labors, whether difficult or easy, were placed on the graph according to their C.O. and transverse diameter. It was found that the greatest change between difficult and easy deliveries fell at a C.O. of 10.0 cm. and a transverse diameter of 12.0 cm. When both the transverse dimeter and the C.O. were over border line (C.O. of 10.0 cm. and transverse of 12.0 cm.) there was difficulty in 0.34 per cent, or 1 in 294 cases. When either the C.O. or the transverse diameter was below border line, the difficulty rose to 1 in 9 cases; and when both were under border line (i.e., C.O. less than 10.0 cm. and transverse diameter less than 12.0 cm.), there was 30.8 per cent difficulty, or 1 in 3.3 cases. This method stresses the importance of the transverse diameter, but generally speaking is probably not too much better than other methods.

TABLE VI. C.O. AND TRANSVERSE OF INLET, PROGNOSIS

C.O. 10.0 CM.	C.O. greater than 10.0 cm. and transverse less than 12.0 cm. 320 cases 10.95% Difficulty	C.O. greater than 10.0 cm. and transverse greater than 12.0 cm. 577 Cases 0.34% Difficulty
	C.O. less than 10.0 cm. and transverse less than 12.0 cm. 52 cases 30.8% Difficulty	C.O. less than 10.0 cm. and transverse greater than 12.0 cm. 35 cases 11.4% Difficulty
	12.0 C.M. TRANSVERSE	

Comment

It seems rather obvious from the results demonstrated above that when the various criteria for inlet contraction are projected into use by another obstetrician their use is somewhat limited. There seems to be only two criteria that are absolute, namely, Allen's area over 130 sq. cm. and Weinberg and Scadron's sum over 25 cm. These are moderately large pelves. Below these levels there are only probabilities. Note that at the other extreme, i.e., small pelves, the range of difficulty is from 1 in 2.4 to 1 in 5. In other words, we cannot do better than Moir's contracted group in which 1 of 2.4 cases will have difficulty. There seems to be only one valid conclusion: In all pelves with vertex presentation, without previous cesarean section, there must be a trial of labor. The handling of a suspect inlet contraction is an art, not a science. This art has become less glamorous, in that with the use of antibiotics, blood transfusions, and the comparative safety of cesarean section after labor, the problem is more easily resolved. This art also encircles the problem of uterine inertia. Uterine inertia is a not uncommon complication of the suspect pelvis. In combination these two problems are not too hazardous for the mother, but may be extremely dangerous to the baby. For this reason one should consider cesarean section earlier in a patient with both uterine inertia and a suspect pelvis, than when the pelvis is normal and uterine inertia is present.

Recent obstetrical literature is stressing the rather high mortality in the premature baby delivered abdominally. In the light of our present inability to determine with accuracy the duration of pregnancy in a given case, the best proof that pregnancy has advanced to its limit is the onset of labor. While this is not directly related to the problem of inlet contraction, it does furnish

an additional argument against elective cesarean section. Actually, the only possible thing in favor of the elective procedure is convenience to the obstetrician.

Recommendations

1. In all patients in whom there has not been a previous cesarean section and in whom there is a vertex presentation, a trial of labor is indicated.

2. Labor will decide whether vaginal delivery or cesarean section is necessary.

3. Lateral pelvimetry during labor will prevent misinterpretation of pelvic findings when molding and caput are present.

4. Antibiotics should be started at the beginning of labor in the suspect pelvis.

5. Uterine inertia and suspect pelvis should be treated by cesarean section.

Conclusions

1. The criteria for inlet contraction cannot be placed on an entirely scientific basis. For this reason trial of labor appears to be indicated in all patients with suspect pelves, who have vertex presentations, and who have not had previous cesarean sections.

2. In abnormal presentations such as breech, clinical and x-ray evaluation associated with obstetrical judgment must be used, since the above methods cannot give an absolute prediction.

The excellent cooperation of the Department of Roentgenology, especially of Drs. W. L. Kilby and C. N. Davidson, the many residents, and Miss Basham, x-ray technician, made this study a pleasant one.

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BUCCAL ANDROGEN ALONE AND WITH ESTROGEN IN TENSION AND ANXIETY

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(From the Mountainside Hospital)

IN PREVIOUS publications[1-3] parenteral and oral estrogen therapy of various gynecologic conditions was described in relation to the effects on vaginal smears. The purpose here is to present the results (1) of androgen therapy in a group of private gynecologic patients suffering from tension and anxiety states due to hyperestrinemia, as revealed by vaginal smears; and (2) of combined androgen-estrogen therapy in a similar group of private gynecologic patients with tension and anxiety whose menopausal smears, either before or following estrogen therapy, indicated varying estrogen effects. The androgen used in this study was testosterone in the form of Oreton buccal tablets. Absorption of the hormone is through the mucous membranes of the mouth. The patient is admonished not to suck the tablet so as to minimize salivary secretion and loss by swallowing. The parenteral estrogens were crystalline estradiol in the form of Micropellets Progynon and the oral estrogen, estrone sulphate.

Material

In the first group, treated with androgen alone, vaginal smears stained according to the Shorr[4] technique were characterized by 80 to 100 per cent of large, discrete, pyknotic, nucleated cells which stained pink, hyperestrin smears. In the second group, treated with estrogen and androgen, the vaginal smears were either menopausal or of variable estrogen effect due to previous estrogen therapy. This group under androgen-estrogen therapy had menopausal symptoms in which anxiety and tension predominated.

All patients in both groups experienced either complete relief or marked reduction in severity of their symptoms. In only a few patients was there any abnormal bleeding or breast congestion. Improvement in sense of well-being was striking. The patients were more capable of concentration, tension and anxiety were lessened, they slept better and depressions and mood variations were greatly relieved. Concurrent administration of the estrogen and androgen prevents breast congestion and uterine bleeding or staining and relieves tension and nervousness not responding to, or made worse by, estrogen alone.

Androgen in the Female

Androgen is normally present in the female, remaining at a fairly constant level throughout sexual life. Gallagher[5] reports the average daily excretion in men as 63 to 68. I.U. and in women 42 to 56 I.U.—figures of the same order of magnitude. Masculinizing effects usually do not follow administration of less than 300 mg. per month. According to Carter, Cohen, and Shorr,[6] the secretory phase of the menstrual cycle is suppressed when androgen is administered during the first half of the cycle. When given after ovulation androgen does not affect the secretory pattern. Androgen does no permanent

damage to the ovaries. Normal pregnancies have followed the use of androgen. Androgen gives increased appetite, better sleeping habits, improved self-confidence, diminished fears, increased libido, and slightly lowered blood pressure, if previously elevated. Androgen relieves tension due to vertex and occipital congestion. In addition to its specific sex effects, androgen is a metabolic catalyst. As an anabolic agent it induces protein formation and retention, stimulating the growth of myometrial elements. Androgen has been used for increased muscular strength in the aging male or female.

Testosterone has about one-twentieth the progestational activity of progesterone. Androgen has an antifibrogenic effect in guinea pigs and in the human being. Androgen inhibits uterine contractions and has constrictive action on myometrial elements. These effects probably account for the use of androgen in dysmenorrhea and metrorrhagia. Androgen sometimes shortens the menstrual cycle by its progestational effect.

The ill effect of overdosage of androgen has been noted in cases of inoperable breast cancer when large therapeutic dosages have been used. Among these effects are edema, drowsiness, sense of ill-being, tinnitus, exacerbation of rheumatic symptoms, hoarseness and other voice changes, tenderness of the nipples, darkened areola, hypertrophy and edema of clitoris and labia, and increased libido.

The oral dose of methyltestosterone (Oreton-M tablets) is approximately 3 times that of parenteral testosterone propionate (Oreton). Absorption of buccal testosterone propionate is more nearly equivalent to parenteral absorption. In the series reported here administration of 150 mg. testosterone per month, given in buccal tablets of 5 mg. daily, was found to be effective clinically and in changing the vaginal smears. No sign of overdosage has resulted from this regimen except a few cases of mild acne, mild hirsuties, and increased libido. Many of the gynecologic conditions amenable to androgen therapy require dosages which completely suppress ovarian function—300 to 500 mg. testosterone propionate per month.

In combined androgen-estrogen therapy, vaginal smears with 0 to 20 per cent cornification may be obtained from 4 mg. crystalline estradiol parenterally plus 150 mg. buccally, or 80 mg. parenterally, testosterone propionate per month. Neutralizing effect indicated by the percentage of cornified cells in the vaginal smear is, therefore, obtained from androgen-estrogen combinations in the ratio of 1 part of estradiol parenterally to 20 parts of testosterone propionate parenterally or 1 part estradiol parenterally to 40 parts testosterone propionate buccally.

Tension States Associated With Hyperestrinemia

The typical patient who shows hyperestrin smears throughout the cycle is the compulsive, high-strung type, whose eyes often show a high luster and whose skin may be moist, flush easily, and frequently show dermographia. The hair is fine and blood pressure normal or slightly elevated. Trapezius myositis is frequently present and there is complaint of occipital pressure and tightness. These patients relax poorly and in spite of their increased psychomotor activity they tire easily. They are the overconscientious, perfectionist type. Anxiety with or without phobias is frequently present. Many have feelings of inadequacy. These patients, premenstrually, are restless and tense, sleep poorly, have sore breasts, are bloated and gain weight from accumulated water in the tissues.

Geist[7] reported relief for 6 months to 2 years in 13 of 20 patients with premenstrual tension treated with 200 mg. testosterone parenterally during the last 2 weeks of the menstrual cycle. Five cases recurred in 6 months and

were given further treatment; 2 were failures. Berlind and also Burlingame and Patterson[8] reported complete relief in 7, partial relief in 3, and no relief in 2 of 12 cases of mastalgia and premenstrual tension from 30 mg. methyltestosterone orally for 2 weeks prior to the menses. Geist and Berlind did not follow the vaginal smears in these studies, so it is probable that failures were cases of hypo-ovaria. These patients usually do well with estrogen from midcycle up to 2 days before onset of menstruation.

As a cause of hyperestrinemia Biskind[9] reports that in presence of vitamin B deficiency, the liver is unable to metabolize estrogens which consequently accumulate in the body. Administration of vitamins alone does not relieve the hyperestrin tension state. High-protein diets may aid in maintaining adequate secretion of androgen by stimulation of the adrenal cortex.

Overdosage of estrogen in treatment of the menopause frequently results in occipital pressure, headache, and tenseness, all promptly relieved by androgen. Excessive estrogen may depress the adrenal as well as the pituitary.

In the first group of 19 patients, whose chief symptoms were anxiety and tension, vaginal smears, taken at different times during the cycle, were of the hyperestrin type. This group was treated with androgen alone in the form of buccal testosterone propionate, doses varying from 100 to 150 mg. per month. Of these patients, 18 were married and the ages were between 32 and 50 years. In 9 patients the menses were scanty, in 4 moderate, in 5 heavy, and in one absent. Tension and anxiety were moderately severe to severe. Of these 19 patients, 13 were observed for 6 to 15 months and the remainder from 2 to 6 months. Androgen dosage in 15 was 150 mg. per month, in one 300 mg., while 3 required 75 to 100 mg. Cornification of the vaginal smears after at least 2 months' therapy was reduced in 15 cases to 20 per cent or less, in 2 cases 25 per cent, and in 2 cases 90 to 60 per cent. The smears were taken at various times during the cycle. Clinical results based upon definite reduction or complete relief of tension and anxiety in 12 were excellent, in 4 good, in 2 fair, and poor in one. One patient, sterile for 8 years, conceived. Marked acne rosacea cleared completely under therapy in 2 patients.

Following are case histories of three of these patients:

CASE 1.—Mrs. A is a 39-year-old housewife with 2 children, aged 7 and 4 years. When seen first in October, 1950, she presented a history of frequent headaches posteriorly and across the eyes, worse premenstrually. She felt keyed-up nervously and complained of tension. When worried or anxious, she showed a generalized tremor. She worried a great deal, particularly about her parents, who were in poor health. She had difficulty in concentrating, was mildly depressed at times and tired easily. The menses were regular and never heavy. Her breasts were frequently sore premenstrually. Previous thyroid treatment had been discontinued since it exaggerated her nervousness. Basal metabolism rate was minus 9. Past history was negative.

Physical examination revealed general healthy appearance, blood pressure 108/72, and negative pelvic examination. Vaginal smears taken at different times of the cycle were consistently at hyperestrin level.

She was placed on a high-protein diet, vitamin B concentrate, and Oreton (testosterone) 150 mg. per month. In one month her symptoms were greatly relieved. The headache was practically gone. She no longer had severe nervous tension and was able to concentrate. She felt stronger in every way. During this therapy the vaginal smear on the eighteenth day of the cycle showed 80 per cent cornification. Androgen therapy was continued at 150 mg. per month until January, 1951, when she was apparently completely well. Menses were regular, there was no headache and no soreness of the breasts. Blood pressure was 182/80. Vaginal smear on the eighteenth day of the cycle showed 20 per cent cornification. Androgen dosage was reduced to 100 mg. per month.

CASE 2.—Mrs. B is 45 years old, a widow, and had never been pregnant. She is employed as a secretary. When first seen, Feb. 20, 1950, she complained of extreme nervousness and tension which were exaggerated pre- and post-menstrually. She felt tired constantly and had episodes of moderate depression. She complained of tension and of a tight feeling in the head. She had a pinkish rash on her face which became very much worse when she was under tension. She stated that she was pleasantly employed.

Previous history was negative except for thyroidectomy for Graves' disease several years earlier. Basal metabolic rate made one year ago was plus 13. Menses were regular and scanty.

Physical examination revealed underweight, tenseness, marked acne rosacea of the face, and dermographia of the neck. Blood pressure was 162/90. Pulse was 90. Pelvic examination was negative. Vaginal smears were of the hyperestrin type in 3 phases of the cycle.

Buccal androgen therapy at a dosage level of 150 mg. per month was continued until May, 1950, at which time vaginal smears were still of hyperestrin type and dosage was increased to 300 mg. per month. Clinical improvement, however, was marked at the lower dosage level. Tension was markedly relieved, acne rosacea subsided, and blood pressure was normal. She slept well and had no headache. On June 1, 1950, vaginal smear was of menopausal type and androgen was reduced to 150 mg. per month. At this dosage level she has remained well and acne has disappeared, tension is relieved, and the vaginal smear remains menopausal in type. The only menopausal symptom is an occasional hot flush. When she was last seen, Jan. 17, 1951, there was no evidence of any masculinizing effect. Dosage was reduced to 75 mg. per month.

CASE 3.—Miss H is 32 years old, first seen in September, 1948. History revealed that due to her mother's poor health she had never been employed. Her fiance was killed in action in 1945. She had been nervous for about 10 years and had a great many phobias and anxieties. Weakness and dizziness were permanent symptoms and when under tension she became nauseated and her hands became cold and moist. At the same time there was an associated frightening feeling of pressure in the chest. A cardiologist found the heart to be normal. She could not travel in buses but would ride in a private car although she would not drive. She was seen by a psychiatrist several times but did not improve.

Physical examination revealed a tense, pale, and nervous patient. The hands were cold and clammy. Blood pressure was 130/74. Basal metabolic rate was normal. Weight was normal and pelvic examination was negative.

Cyclical estrogen therapy for several months gave slight improvement in the nervousness but increased the feeling of pressure in the chest and caused breast congestion. Vaginal smears showed hyperestrin level of 75 to 100 per cent cornification and estrogen therapy was discontinued. In November, 1949, buccal androgen therapy was begun at 150 mg. per month. Under this therapy she has shown marked improvement. She has regained self-confidence and has learned to drive a car. Pressure in the chest is practically gone and, when it appears, she simply takes an additional 5 mg. Oreton Buccal Tablet. She lives an active social life and is free from previous anxieties and phobias. Vaginal smears at several recent examinations show reduction from hyperestrin level to 20 per cent cornification.

The second group of 20 patients had been under treatment for hypo-ovarian symptoms of the menopause. Tension and anxiety had not been adequately relieved by estrogen alone. These patients were given a combination of estrogen and androgen. The estrogen used was crystalline estradiol parenterally in 14 patients and oral estrone sulfate in 6. Testosterone was given buccally in 18 and parenterally in 2 patients. Ages varied from 34 to 54 years. Five patients had had hysterectomies, 5 had menopausal amenorrhea, and the remainder menstruated regularly, none heavily. Anxiety and tension symptoms were severe in 80 per cent of these cases. All of the patients except one showed more

marked relief with the combination of estrogen and androgen than with estrogen alone. With estrogen alone relief of symptoms due to hypoestrinism occurred at a vaginal smear level of 20 to 100 per cent cornification: with estrogen and androgen together those patients whose vaginal smears showed as low as 10 per cent cornification felt well, as also did 6 patients in whom the androgen neutralized the estrogen completely, showing no cornification in the vaginal smear. The vaginal smear is, therefore, not a reliable index of the clinical results. Ratio of estrogen to androgen for symptom relief varies with potency of the hormones and with route of administration, oral or parenteral. Individual variations from patient to patient depend on whether the ovaries are present, absent, functioning poorly or not at all, whether the adrenal gland is functioning normally, subnormally, or hypernormally, and whether nutritional factors are normal. In this series it was found that 4 mg. crystalline estradiol monthly was neutralized, as shown by vaginal smears, by 150 mg. buccal testosterone propionate in 2 patients. In 4 patients the androgen reduced the cornification to a menopausal level at an estrogen-androgen ratio of 1:40. Testosterone propionate by parenteral injection gave a corresponding neutralizing ratio of about 1:20. With estrone sulfate and buccal testosterone the neutralizing ratio is from 1:2 to 1:7 and with estrone sulfate and testosterone propionate the neutralizing ratio was from 1:1 to 1:3.5. Dosage of oral methyltestosterone (Oreton-M Tablets) should be about 3 times the parenteral dose. It is advisable to bear these various ratios in mind when prescribing a combination of estrogen and androgen.

One patient apparently did better on estrogen alone than with the addition of androgen. On combined therapy she showed facial hirsuties, mild acne, restlessness at night, hot flushes, and general aching. These symptoms disappeared upon discontinuance of the androgen.

Staining occurred in 2 patients and was difficult to control. In one it was controlled by increasing the androgen and reducing the estrogen. In the other, testosterone propionate, 50 mg. daily parenterally for several successive days, failed to control the bleeding and dilatation and curettage were necessary. One patient, who had had a hysterectomy for endometriosis, was getting too much estrogen (estrone sulfate 45 mg.) and too little androgen (buccal testosterone propionate 150 mg. monthly) and felt very tense and nervous. The vaginal smears showed 60 per cent cornification. With discontinuance of estrone sulfate symptoms were controlled. In the presence of fibroids and endometriosis androgens should be used in greater ratio than in patients without these complications.

Following are case histories of two of the patients of this series:

CASE 1.—Miss B. is 51 years of age. She was first seen for her present illness in October, 1950. Menstruation had been very irregular for 2 years, every 3 or 4 months and never heavy. She felt mentally confused, had difficulty in concentrating, slept poorly, was extremely tense, nervous, and irritable, had frequent flushes, had lost interest in social contacts and felt depressed and apathetic. She had quit her job and since it was not financially necessary for her to work, was staying home with her parents. She had previously led a normal life with many social activities. She had worked in a business office for 12 years.

Previous history was negative except for appendectomy in 1931. She had had treatment at infrequent intervals for *Trichomonas vaginalis* infection.

On physical examination she appeared tense and anxious. Blood pressure was 132/84. The uterus was small and anteflexed. The vaginal smear was menopausal in type. Therapy was begun with parenteral estradiol 1 mg. once weekly. One month later improvement was beginning but breasts were sensitive. Dosage was increased to 2 mg. and

testosterone propionate 10 mg. was given parenterally concurrently once weekly. In one month the vaginal smear showed 80 per cent cornification and nervous symptoms were markedly relieved. She felt stronger, was able to concentrate better, slept well, was no longer depressed, had had no headache, and was back to her normal activities.

CASE 2.—Mrs. H. B. is 38 years of age. She was first seen in April, 1947, complaining of severe nervousness and tension. She had recently moved here from the Middle West and her husband was away on business a great deal. She had 3 children aged 15, 9, and 4½ years. Menses were heavy and prolonged. Five years previously she had been in a psychopathic hospital for 10 days with depression and amnesia. One year prior to this she had had a duodenal ulcer. Her heavy menses had been treated unsuccessfully with progesterone and in September, 1947, she had had a dilatation and curettage, which also failed to control the bleeding. Therefore, in February, 1948, hysterectomy was performed and a fibroid uterus removed. When seen again in December, 1949, she complained of extreme weakness, depression, general nervousness with frequent tremor and tightness and pressure in the head and back of the neck. At times she felt very energetic.

Examination at this time showed moderate malnutrition. Blood pressure was 142/84. Breasts were normal. Vaginal smear was of menopausal type.

Therapy with estrone sulfate 2.5 to 3 mg. daily was begun. There was mild improvement but the severe tension was not relieved and the pressure in head and neck was intense. Vaginal smear showed 25 per cent cornification. When seen in September, 1950, she had been taking estrone sulfate 5 mg. daily and was very depressed, crying easily, and very tense. Vaginal smear showed 100 per cent cornification. Therapy with buccal testosterone propionate 300 mg. with estrone sulfate 150 mg. per month was begun. One month later she felt fine, depression was entirely gone. She did not tire, slept well, and head tension was gone. She had not felt so well in years. At the end of December, when seen again, she was feeling just as well. She was continuing therapy and the vaginal smear showed 90 per cent cornification.

Summary

Two groups of patients showing tension and anxiety symptoms have been presented. In one group, with vaginal smears indicating hyperestrinism, androgen alone was used with favorable results. The other group, previously treated for hypo-ovaria or menopausal symptoms with estrogen alone without relief of tension, was given estrogen-androgen therapy with excellent results.

Buccal tablets of testosterone propionate (Oreton Buccal Tablets) were used. Buccal dosage should be approximately twice parenteral dosage. Optimal neutralizing estrogen-androgen, as revealed by percentage of cornified cells in vaginal smears, is 1:40.

Androgen alone and with estrogen has a definite place in gynecologic therapy. This field should be further explored. Androgen is effective in dosages less than those producing masculinization.

Testosterone propionate buccal (Oreton Buccal Tablets), testosterone propionate parenteral (Oreton), methyltestosterone oral (Oreton-M Tablets), crystalline estradiol (Micropellets Progynon) and ethinyl estradiol (Estinyl Tablets) were supplied, in part, by Schering Corporation, Bloomfield, New Jersey.

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THE PRECLINICAL RECOGNITION OF TOXEMIA OF PREGNANCY*

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EVER since the medical profession first recognized the clinical syndrome known as toxemia of pregnancy, there has been a constant search for a means of determining which patients might be prone to develop this entity before the time of appearance of clinical symptoms. Attempts have also been made to develop a method which, when applied to patients who have suffered with previous toxemia of pregnancy or who have had pre-existing cardiovascular-renal disease, would predict or prognosticate their ability to withstand subsequent pregnancy without a recurrence or exacerbation. We believe we have found such a method, which has promise of achieving these objectives. In this paper we shall present the evidence obtained to date in support of this probability.

This study originated in February, 1950, after one of us (H. M. B.) heard a presentation made by Krasno and Ivy[1] in 1949. These authors described a method for determining, hypothetically, the presence of vasospasm or vasomotor hypertonus in the ocular fundus. In their report they alluded to several patients who had suffered from pre-eclamptic toxemia, along with their more exhaustive study of other vasospastic conditions of a medical nature. These authors felt that they could predict the subsequent development of a more serious vascular disease, and possibly of an impending vascular accident by measuring the response of the retinal vessels to a small dose of nitroglycerine, the condition of the retinal vessels being only an indicator of a generalized vasomotor hypertonus. Since vasospasm is an integral part of the general picture of toxemia of pregnancy, it was believed that with a sensitive test we could determine the presence of such spasm in a pregnant woman. Therefore, we could predict the appearance of a subsequent toxemia if the patient had not been afflicted with a previous disease to explain the vasospasm.

This presentation is a preliminary report which provides the results obtained on a relatively small number of patients during a rather short period of time. Nevertheless, the observations were so uniformly predictive that we felt it appropriate to call them to the attention of other observers in order to obtain a wider use of the test, and thus a better evaluation of its potentialities. If our observations to date are corroborated by a more extensive study by us and by other investigators, we shall have a method of determining whether a patient will develop toxemia of pregnancy before the appearance of any of the now-established clinical signs of that disease. Furthermore, we shall have a method of ascertaining whether our management designed to prevent the development of a clinically frank toxemia is effective. Therefore, we urge others to take up

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this study and help amass sufficient material either to prove or disprove the present apparent potentialities of this test.

Method

In performance of the test, the apparatus designated as the Krasno-Ivy flicker photometer is used. This machine measures the visual threshold for the fusion frequency of flicker, or the ability of a person to recognize flicker. By this is meant the phenomenon whereby a normal individual will see as a steady source of light the ordinary light bulb which actually flickers at the rate of 60 times per second. If the frequency of the flicker is gradually reduced it will eventually be detected by the observer, usually when the rate, depending on the light intensity, reaches about 40 per second, although the actual rate differs for each individual and may vary in the same individual due to various factors. However, for a period of minutes up to several hours and unless the environment of the patient is changed, the ability to recognize flicker remains very constant. The resulting measure in flashes per minute is called the Flicker Fusion Threshold or F.F.T. The shortened designation, F.F.T., will be used through the remainder of this report.

The photometer is so constructed that the frequency of the flicker can be increased or decreased, and the rate of flicker per minute at any point can be read on a dial.

The test, as conducted on the Krasno-Ivy flicker photometer, is designed to detect ocular vasomotor tonus as it is affected by the administration of nitroglycerine. The patient is seated in a resting position for ten minutes before testing is begun. Smoking is to be avoided for six hours preceding the test and alcohol must not have been used during the previous twenty-four hours. Medication with hypnotics, vasodilator drugs, or analeptics must be considered in the interpretation of the results. If the patient normally wears glasses, these should not be removed for the test. Binocular vision is always employed. The patient is seated 1.6 meters from the frosted-glass illuminated viewing window, the distance being accurately obtained by measurement with the cord attached to the machine.

The action of the machine is first explained to the patient and she is instructed to say "Yes" as soon as flicker in the light is detected. Several trial readings are taken in order to accustom the patient to the action of the machine, then three successive readings are obtained as the "normal" base line for that patient. The patient is told to report flicker just as soon as she thinks the light is flickering and that she should not debate the question whether it is or is not flickering. When these precautions are taken it is surprising how accurate and constant these readings are for each individual, and how little any of the readings will vary from each other. A tablet of $\frac{1}{100}$ grain nitroglycerine is then administered sublingually, the patient being told to allow the tablet to dissolve without swallowing. Two minutes are allowed for dissolution and absorption of the drug and another series of three readings is then made at two-minute intervals and recorded. If no appreciable difference is noted between these and the original, or control readings, after six minutes, another tablet of nitroglycerine is given and the routine of the three tests is repeated.

In normal subjects the use of nitroglycerine will produce a dilatation of the arterioles and congestion of the retina with a resulting impairment of the ability to recognize flicker which is indicated by a lower F.F.T. We shall henceforth refer to this as a negative, or normal, test. In vasospastic individuals, the retinal vessels will dilate under the influence of the nitroglycerine, the blood flow and oxygenation of the retina will be improved, and the F.F.T. will rise;

in other words, the ability to recognize flicker will be improved, resulting in what we shall designate as a positive, or abnormal test.

Patient Material

The patient material studied was derived from several different clinics in Chicago in order to accumulate observations more rapidly. Patients attending the prenatal clinics of the Mount Sinai and Presbyterian Hospitals were tested routinely. In addition to this, private maternity patients were made available for use by the members of the attending staffs of these hospitals because they showed evidence of toxemia or of cardiovascular-renal disease or had previous histories of any of these entities. It must be emphasized that, since the patients in this latter category had been deliberately selected for this study, we can make no statistical report on the frequency of toxemia because we have intermixed the two groups of patients tested.

Observations

There was a sufficient number of normal, or negative tests in our routine prenatal clinic testing to allow us to make several statements of fact. The F.F.T., in our experience, is not affected by pregnancy, parity, month in pregnancy at which the test is made, age, race, national origins, "nervousness" or excitability, anxiety, weight, or marital status. In all we have conducted 400 tests on 199 patients. Of these, 161 showed consistently normal responses and can be considered as controls. These patients are of no further interest in this report. Thirty-eight patients showed abnormal, or positive responses. These we shall discuss further (Table I).

TABLE I. RESULTS OF F.F.T. TESTS

NO. OF PATIENTS	NO. OF TESTS	PATIENTS WITH POSITIVE TESTS	PATIENTS WITH NEGATIVE TESTS
199	400	38	161

First, the most interesting group was the one in which we obtained abnormal (positive) tests on patients who, at the time of the test, showed no clinical signs of toxemia and who had no past history of toxemia of pregnancy or of cardiovascular-renal disease. There were 23 patients who fell into this classification. Of these, 10, or 43 per cent, later developed clinical signs of toxemia of pregnancy varying from mild to the convulsive type. The other 13 patients in this group are as yet undelivered. Thus far in our study, no patient has yielded a positive test who did not have pre-existing disease or who did not subsequently develop signs of toxemia of pregnancy, except for those in the undelivered group, the outcome of which we do not yet know. This is the most significant part of our work. With our test being positive before the appearance of edema, proteinuria, and hypertension, we presume to think that we predicted that these clinical signs would occur by the fact that we had previously obtained the positive test. In those patients in this group whom we studied further, and on whom retinoscopy and blood chemistry studies were made, there was also no indication of abnormality by any of these tests. The time lapse between our determination of a positive test and the appearance of clinical signs varied from two to eight weeks, the average being 4.6 weeks (Table II).

Second, it was found that every patient who came to the clinic with actual clinical signs of toxemia of pregnancy showed a positive F.F.T. There were eight patients in this group.

Third, up to date, no patient who has shown consistently a normal response, has subsequently developed toxemia, and no patient who has presented clinical signs of toxemia has given a normal test.

TABLE II. PATIENTS WHO SHOWED A POSITIVE F.F.T. AND LATER DEVELOPED SIGNS OF TOXEMIA OF PREGNANCY

PATIENT NO.	LENGTH OF TIME BETWEEN POSITIVE F.F.T. AND DEVELOPMENT OF SIGNS OF TOXEMIA
1	5 weeks
2	3 weeks
3	4 weeks
4	2 weeks
5	3 weeks
6	5 weeks
7	4 weeks
8	8 weeks
9	6 weeks
10	6 weeks

TABLE III. POSTPARTUM F.F.T. TESTS ON PATIENTS SHOWING POSITIVE (ABNORMAL) TESTS

PATIENT NO.	LENGTH OF TIME POST PARTUM	TEST RESULT	PATHOLOGY AND REMARKS
1	8 weeks	Negative	Mild pre-eclamptic toxemia
2	6 weeks	Negative	Mild pre-eclamptic toxemia
3	1 hour	Positive	Ergot reaction
	24 hours	Negative	
4	5 months	Positive	Normal blood pressure and urine. Severe toxemia of pregnancy. 35 years old.
5	6 weeks	Positive	Vascular hypertension
	5 months	Positive	
6	4 weeks	Positive	Vascular hypertension 150/80
7	5 weeks	Positive	Nephritis
8	3 months	Positive	Severe fulminating toxemia of pregnancy
9	4 weeks	Negative	Pre-eclamptic toxemia
10	2 days	Positive	True eclamptic. Positive
	6 weeks	Negative	F.F.T. two months before clinical signs
11	7 weeks	Positive	Vascular hypertension
12	6 weeks	Negative	True pre-eclampsia
13	2 days	Negative	True pre-eclampsia
14	3 weeks	Positive	Vascular hypertension

Fourth, 14 patients who showed antepartum toxemia or cardiovascular-renal disease with positive F.F.T. were studied after delivery. Six of these patients had reverted to normal, while eight still showed positive, or abnormal tests (Table III). Table III shows the testing results on these patients with their underlying pathology. Patient No. 13 had a true toxemia which was detected six weeks before delivery by a positive F.F.T., while the clinical signs did not appear until she went into labor. Her test was negative two days post partum when her blood pressure had reverted to 120/70. Patient No. 10 had a true eclamptogenic toxemia in labor. Her F.F.T. was positive three months before delivery and two months before she developed any clinical signs of toxemia. The F.F.T. was still positive two days post partum, but had become normal six weeks post partum. Patient No. 4 was tested five months after a premature delivery at seven months' gestation with a very severe toxemia; although her blood pressure was 110/70 and the urine was negative, her flicker test was positive.

Fifth is that group of patients with pre-existing cardiovascular-renal disease whom we tested during pregnancy and who were found to give abnormal tests. All of these women retained their positive F.F.T. post partum. Patients Nos. 5, 6, 11, and 14 fall into this category because of vascular hypertension or so-called "essential hypertension." Patient No. 7 is a true nephritic who is now in an acute exacerbation of her nephritis. Patient No. 3 had a normal antepartum F.F.T. and no clinical signs of toxemia throughout pregnancy or labor. After the administration of ergotamine intravenously, the blood pressure suddenly rose to 170/100 and the F.F.T. became positive. Twenty-four hours later the blood pressure was normal and the F.F.T. was negative. We consider this as evidence of a sensitivity to ergot; a problem we hope to explore in the near future. Patient No. 8 had an acute fulminating toxemia of pregnancy and has retained her positive F.F.T. three months post partum.

As yet, we are unable and unwilling to state that the degree of abnormality in the test is significant or indicative of the imminence or the severity of the toxemia that may develop. We can say, though, that an increase of 30 flickers or more per minute must be considered a positive test.

Comment

In view of the observations here presented, we believe that we may draw certain tentative conclusions and present certain assumptions and speculations. However, because the number of patients is relatively small, and because we have been engaged in this study for a relatively short time, we shall be cautious in these conclusions. Nevertheless, the striking results obtained prevent us from being uncourageously modest in our claims. Since 161 patients who had normal tests completed their pregnancies without incident as far as toxemia is concerned, we feel safe in stating that any patient who shows several normal F.F.T. tests, especially in the third trimester of pregnancy, can be safely assured, from a statistical viewpoint, that she will not develop pregnancy toxemia.

Conversely, a patient who displays a positive, or abnormal test during the course of a pregnancy has either pre-existing cardiovascular-renal disease or will develop toxemia of pregnancy before she reaches term. Since most women with pre-existing vascular lesions or previous toxemia of pregnancy are aware of this and will tell of it during the course of their history taking, we can, statistically, assume that ostensibly normal women who, during pregnancy, develop positive F.F.T. tests will show signs of toxemia before delivery. Confirming this theory to a further extent is the group of women who presented themselves for testing after having developed the clinical signs of toxemia of pregnancy. All patients in this latter group gave positive tests.

An interesting point for speculation and further study comes to light in our résumé of Table III. All but two of the patients who had true toxemia of pregnancy reverted to a normal test in the interval of two days to eight weeks post partum, while the true cardiovascular-renal group retained their positive F.F.T. Does this fact indicate that true toxemia does clear up completely and leaves no residual damage? Do the two patients who had positive tests three and five months post partum have true vascular disease?

To indicate the possible usefulness of the test in measuring the patient's response to the management of the toxemia, we shall cite the following case history:

An 18-year-old gravida ii, para i, with a positive F.F.T. and no clinical signs of toxemia, ten days following the test developed albuminuria and edema. She retained her positive flicker test when these signs appeared, and was placed on bed rest, phenobarbital,

methionine, potassium chloride, and salt-free diet for two weeks. After this period of treatment the clinical signs disappeared completely and the flicker test reverted to normal. This patient delivered spontaneously without a return of any of the signs or symptoms of toxemia. The flicker test at the time of delivery was still negative or normal.

In view of this evidence, and with a plea to help us answer these questions, we ask other investigators to take up this work. We think that we are justified in stating that the nitroglycerine flicker fusion test as determined by the Krasno-Ivy flicker photometer will detect the predisposition to toxemia of pregnancy and will provide a method for the preclinical recognition of this disease entity before it can be detected by clinical signs, direct retinoscopy, or blood chemistry changes. We recommend an exhaustive, carefully conducted study of this test in order that a complete evaluation of its efficacy may be determined.

Conclusions

1. The Krasno-Ivy flicker photometer is a reliable apparatus for determining the flicker fusion threshold.

2. The nitroglycerine flicker fusion test proposed by Krasno and Ivy is a valuable aid in the detection of vascular spasm induced by toxemia of pregnancy.

3. By using this test we have predicted the development of toxemia of pregnancy two to eight weeks before the ordinarily recognized signs and symptoms of toxemia of pregnancy appeared.

4. A positive, or abnormal test before the advent of clinical signs of toxemia of pregnancy, with adequate prophylactic therapy, may allow us to forestall the onset of the toxemia.

5. The use of the test assists in estimating the adequacy of the management of the patient.

The authors wish to acknowledge the great encouragement, advice, and help given them by Drs. L. R. Krasno, A. C. Ivy, and E. D. Allen.

The authors also wish to acknowledge the aid given them by the Clinical Instruments Company of Chicago, the manufacturers of the Krasno-Ivy flicker photometer, who provided them with the instruments used for this study.

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Discussion

DR. EDWARD ALLEN, Chicago.—These observations just reported have been the most exciting thing that has happened on our Obstetrical Service at Presbyterian Hospital in many years. Everyone from the nurses and student clerks to the senior members of the attending staff are talking glibly now in terms of the "Flicker Fusion Test." Many times in the past months I have heard a discussion of an interesting case begin in the hall or in our doctors' room and one of the first questions to be asked is, "How's her flicker?" The frequency and manner in which this question is asked graphically demonstrates the excitement which everyone feels—that this may be it! For the first time we may have a dependable aid in foreseeing pre-eclampsia or eclampsia as well as a dependable guidepost for us in advising those patients who come in advance concerning future conceptions, especially those who have had cardiovascular-renal trouble during previous pregnancies.

I would like to pay my compliments to Dr. Ivy for his share in developing the photometer as a general diagnostic tool. Dr. Brill deserves a great deal of credit for initiating this investigation and for asking his collaborators to pool their results with his so that an evaluation of this test could be arrived at more quickly. More of this type of cooperative effort is desirable for the rapid advance of our medical knowledge.

The results given in this paper are almost too good to be true. When any laboratory test approaches 100 per cent in accuracy we must maintain an attitude of healthy skepticism until sufficient time has elapsed and a large enough number of results have been recorded either to prove or to disprove enthusiasm. The backlog of results obtained in general cardiovascular disease and reported during and since 1948 by Drs. Ivy, Kranso, and their co-workers cannot be transferred directly to obstetrical patients. They do, however, suggest strongly that the acute vasospasm, which we have known for years exists in toxemia of pregnancy, may not only allow us to prognosticate this disease in its incipiency, treat it early, but perhaps will help us to clarify some of the confusing points in its classification.

It would seem that to evaluate this test properly it will have to become a part of the regular armamentarium in our offices and the clinic.

The preliminary checking done on all of our patients under study for sterility, in addition to those healthy young women who come for premarital or prepregnancy advice, would quickly form our fundamental control group. Repeated checking during the ensuing pregnancies and puerperium should enable us to record the impact of gestation on their vascular systems as well as its involution during the postpartum period. I am reasonably sure that a considerable number of these enterprising young women would quickly not only develop pregnancy but toxemia as well and that it would enable us to beat Dr. Ivy to the prognostic tape on his bad coronaries.

It would be of interest to know whether with further experience we may be able to differentiate with this diagnostic tool between the essential hypertensive, due to previous glomerular nephritis, and the pure toxemia of pregnancy. It is interesting to note that the vasodilatation due to nitroglycerine is an integral part of the test and yet veratrum viride which we formerly gave to decrease blood pressure during toxemia has no effect on the Flicker Test. The measurable production of vasospasm by nicotine may not cause many of us to quit smoking but it may point the way for localizing the action of many drugs on the vascular system and its innervation.

Future investigation along this line may not only give us a lead as to the end organs involved in the response to toxemia of pregnancy but a measure as to the method of action and effectiveness of drugs used in its treatment.

DR. WILLIAM J. DIECKMANN, Chicago.—This work of Dr. Brill and co-workers is of great significance if it can be confirmed. They state correctly that their series is much too small. Dr. Krasno has demonstrated the instrument and I considered it worth while investigating. However, the war left us short-staffed and I had no one who could devote sufficient time to the use of the instrument.

I hope Dr. Brill and his associates will follow up their patients who gave a positive flicker test because if pre-eclampsia-eclampsia is primarily a disturbance in water and electrolyte balance, the patient should not have subsequent evidence of vascular-renal disease and should not have a recurrence in subsequent pregnancies.

I have believed for many years that the vascular spasm is a late manifestation of pre-eclampsia and would anticipate that those patients having a positive flicker test would ultimately have essential hypertension.

THE EYE GROUNDS DURING TOXEMIA OF PREGNANCY

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THE purpose of this article is threefold: (1) to present 100 cases of toxemia of pregnancy with study of the eye grounds; (2) to compare them with similar studies made previously; and (3) to discuss the relationship of the ophthalmoscopic findings to the course of the systemic disease. In describing my cases, I have introduced new criteria and elaborated others.

Type of Patients Studied: Method of Study

The patients studied had been admitted to the Margaret Hague Maternity Hospital with a diagnosis of toxemia of pregnancy or eclampsia. The criteria for selecting these patients are given below, quoted from Burnett and Hamel.[1]

1. Hypertensive: Prior to the twenty-fourth week of pregnancy, diastolic blood pressure of 90 or over and/or systolic blood pressure of 140 or over.
2. Pre-eclampsia: After the twenty-fourth week of pregnancy. Diagnosed when one or more of the following are present:

a. Diastolic blood pressure of 90 or over and/or systolic blood pressure of 140 or over at two readings six hours apart, diastolic pressure being taken when the sound changes and not when it disappears.

b. Albuminuria (trace or more) present in two catheterized specimens collected six hours apart, in the absence of pyuria or hematuria.

c. Edema in exceptional cases, either obvious or occult, as evidenced by excessive weight gain due to water retention (almost always occurs in conjunction with hypertension or proteinuria or both).

d. If diastolic pressure of 90 or over and/or systolic pressure of 140 or over is present at one reading, *and* either edema or albuminuria in one catheterized specimen is present.

3. Eclampsia: Convulsions accompanied by some or all of the signs of pre-eclampsia.
4. Unclassified: Those cases which because of insufficient or inconclusive data cannot be classified as above during the course of pregnancy or puerperium, or during eight weeks' postpartum observation.

With the use of the above criteria for selecting patients with toxemia of pregnancy, Table I shows the ratio of Negro to white and the group according to age and gravidity. The eye grounds of the group described in Table I were studied twice a week. At first the pupils were dilated by instilling a mydriatic, but after about seventy-five cases were studied it was found that mydriasis could be avoided as the changes were almost invariably near the disc. However, if the pupils were small homatropine mydriasis was used.

The examination involved careful scrutiny of the retinal vessels, especially the arterial tree, a search for hemorrhages, exudates, edema, and retinal detachment. In evaluation of the vessels, particular attention was paid to the caliber of the arterioles. Segmental alterations were important and easy to

TABLE I. TABULATION ACCORDING TO AGE, RACE, AND GRAVIDITY

	NEGRO	WHITE	UNDER 20 YEARS	20-30 YEARS	30-40 YEARS	OVER 40 YEARS	GRAVIDA i	LESS THAN GRAVIDA vi	MORE THAN GRAVIDA vi
No. of Cases	25	75	18	42	38	2	45	45	10

detect. Whether these alterations in caliber are due to spasms or sclerosis is difficult to say in all instances, for doubtless the latter is often a transition from the former.

In reference to arteriolar changes as sclerosis, the following criteria were used: Sclerotic changes such as arteriovenous nicking or decreased transparency of the vein through the artery at the arteriovenous crossing was considered indicative of sclerosis. More important, segmental arteriolar narrowing of an irregular, rough-looking type, not sharply demarcated at its limits, was considered focal arteriolar sclerosis.

On the other hand, segmental narrowing of a smooth, regular type, with precipitous limits, and no other vascular changes (such as arteriovenous nicking) was considered indicative of arteriolar spasm. Variations in the light reflex were not found to be of particular value. The changes due to spasm or sclerosis or both are referred to as "focal arteriolar changes."

The over-all caliber of the arteriolar tree was then compared with the normal and the venous diameter in the same eye. Estimations of the caliber of an arteriole as a whole were difficult and small variations were impossible to detect with accuracy. The comparison of the over-all caliber (in contradistinction to segmental changes) of an arteriole to the over-all caliber of the adjacent vein is referred to as the "arteriovenous ratio."

In estimation of the arteriovenous ratio several factors must be kept in mind when the alteration is not marked. To begin with, frequently there are no vessels fit for comparison. Unless the vessels are comparable to begin with, no comparison can be made. A comparison of the diameter of the inferior retinal vein with the inferior temporal retinal artery because they are adjacent is not valid as an arteriovenous ratio, especially when attempts at evaluating small changes are being made. It might be said that the arteriovenous ratio should be evaluated farther to the periphery where similar vessels are present. Similar branches might be encountered adjacent to each other in the periphery but branching has occurred several times. Branching is not regular by any means, so that although segments of similar branches of the arteries and veins are adjacent in the periphery, the ratio in the normal individual need not be artery-two, vein-three.

Often the venous tree is more full than usual or narrower, presumably on a developmental basis; the same may be said of the arteriolar tree.

When the generalized arteriolar narrowing is marked or when the arterioles are normal, the arteriovenous ratio is helpful. In my opinion, small variations in the caliber of an arteriole over a large segment or over the entire arterial system are nearly impossible to detect by simple inspection with the ordinary hand ophthalmoscope, even with the Lambert[2] graticule.

In this study, changes in the arterioles of a focal type were stressed and generalized narrowing, especially of small amounts, was not considered very reliable. When early changes only are noted, several observations are essential to determine the phase of the process we are dealing with. However, the occurrence of hemorrhages, white flecks, retinal edema, or detachment is significant, when first encountered.

When the findings are confined to the vessels alone, observation is necessary to determine the phase of the retinal vascular disease. Three possibilities exist: the condition will remain static; it will regress; or it will become worse. If the picture is static, then the vascular changes might be due to a disease process now inactive (such as previous toxemia of pregnancy) or vascular changes might be due to another disease process such as essential hypertension or renal disease. On the other hand, pre-eclampsia might be the etiological factor, and the conservative management has altered the course of the disease favorably. Regression of vascular changes was observed only three times and these times the changes were probably of a functional nature. Presumably, these patients had pre-eclampsia and conservative therapy was effective. Eye ground changes which develop during toxemia of pregnancy in the last trimester, or changes already present which get worse, are probably due to the toxemia in nearly every instance. Except where retinopathy, retinal detachment, or definite arteriolar spasm is encountered, it is incorrect to form an opinion on one study of the ocular fundi. This is of fundamental importance; it has not been stressed.

Another phase of the study included history, physical examination, and laboratory studies on each patient. In the history, family history of high blood pressure, previous toxemia of pregnancy, renal disease, and high blood pressure were noted. The outcome of the pregnancy was noted.

A very important part of the examination was the blood pressure determination. In order to introduce standardization, the blood pressure was taken as the average of a few (two to four) days before delivery when possible. If the blood pressure increased on treatment, the highest reading was taken. On a few occasions the only determination was one taken in labor.

Laboratory studies included routine urinalysis, quantitative urinary protein determinations, urea and uric acid clearance tests, and others as indicated.

Findings

In the one hundred patients studied, twenty-seven showed fundus changes of an incontroversial degree. These changes included focal arteriolar changes such as spasm or sclerosis, hemorrhages, white flecks, edema of the retina, and retinal detachment. In no instance was generalized narrowing of the arteriolar tree or one of its branches sufficient to warrant positive diagnosis. In this group most of the changes were focal arteriolar in type. Retinopathy and detachment due to toxemia of pregnancy were not common (Table II).

TABLE II. OPHTHALMOSCOPIC FINDINGS

	FOCAL ARTERIOLAR CHANGES	RETINOPATHY	EDEMA OF RETINA	RETINAL DETACHMENT
No. of Cases	27	3	1	1*

*One patient had an idiopathic detachment of the retina which was successfully operated upon. She was not included in the series.

The incidence of positive eye ground changes according to race, age, and gravidity is shown in Table III. The occurrence of positive eye ground changes is about the same in Negro and white women according to this group. Also it appears that positive eye ground findings are more likely to occur in older patients.

Urinary findings such as albuminuria, changes in urea clearance and uric acid clearance show no significant relationship to the presence of positive eye ground changes (Table IV).

TABLE III. RELATIONSHIP OF PERCENTAGE OF FUNDUS CHANGES ACCORDING TO RACE, AGE, AND GRAVIDITY

	NEGRO	WHITE	UNDER 20 YEARS	20-30 YEARS	30-40 YEARS	OVER 40 YEARS	GRAVIDA i	LESS THAN GRAVIDA vi	MORE THAN GRAVIDA vi
Without fundus change	19 76%	54 72%	17 94.5%	33 78.6%	22 57.9%	1 50%	34 75.6%	34 75.6%	5 50%
With fundus change	6 24%	21 28%	1 5.5%	9 21.4%	16 42.1%	1 50%	11 24.4%	11 24.4%	5 50%

TABLE IV. THE INCIDENCE OF FUNDUS CHANGES RELATED TO URINARY FINDINGS

	ALBUMINURIA	DECREASED UREA CLEARANCE	DECREASED URIC ACID CLEARANCE
Without fundus changes	25, or 34.2%	10, or 18.1%	25, or 50%
With fundus changes	16, or 59.1%	0 0%	10, or 52.6%

By the criteria given before for recording blood pressure, it was found that the incidence of pathologic eye ground changes increased with the height of the blood pressure. It is noteworthy that positive eye ground changes were present in patients with blood pressure under 140/90 (Table V).

TABLE V. THE RELATIONSHIP OF THE FUNDUS FINDINGS TO THE ELEVATION OF THE BLOOD PRESSURE

	LESS THAN 140/90	MORE THAN 140/90 AND LESS THAN 175/125	MORE THAN 175/125
Without fundus changes	57, or 87.6%	16, or 55.1%	0, or 0%
With fundus changes	8, or 12.3%	13, or 44.8%	6, or 100%

In Table VI the findings of other authors are presented. There is wide variation, yet the findings of Schultz and O'Brien are strikingly similar to mine.

TABLE VI. FINDINGS OF OTHER AUTHORS

AUTHOR	DATE	PERCENTAGE OF POSITIVE EYE GROUND FINDINGS	NO. OF CASES	COMMENT
Wagener[3]	1933	70	40	Location of changes not stressed
Masters[4]	1933	100	206	A diffuse process
Gibson[5]	1938	79.4	39	Changes mostly peripheral and diffuse, especially early
Schultz and O'Brien[6]	1938	26	145*	Changes mostly central
Hallum[7]	1947	100	2500	Changes mostly central and focal

*The figures presented were selected in order that they might compare with the type of patients in my group.

There are several reasons for the wide variation in findings. First, the type of patients selected for study is not uniform. Second, we are dealing with subjective interpretation of borderline changes, especially in the evaluation of early eye ground alterations.

Interpretation of Findings

The evaluation of eye ground changes is helpful in the management of patients with toxemia of pregnancy. This is especially true when the changes are due to activity at the time of examination. Pathologic eye findings known to originate or to progress during toxemia of pregnancy have a definite meaning. Strictly speaking, such changes in the eye grounds mean that at least one part of the vascular tree (and that part mostly arteriolar or precapillary arteriolar) is undergoing changes of a specific type and amount. There is no good reason to believe that the eye ground changes observed are part of an even diffuse process evident throughout the entire vascular tree, or that retinopathy indicates marked organic changes in the kidney, brain, splanchnic bed, and heart.

This notion is of fundamental importance in discussion of the problem of the relationship of the eye ground findings to general disease. Wagener studied muscle biopsies in a patient with toxemia of pregnancy and found organic vascular disease in one patient. However, Castleman and Smithwick[8] took kidney biopsies in one hundred patients with hypertension and found that organic vascular kidney disease was absent in 28 per cent of cases, and only mild changes were present in an additional 25 per cent when there were positive eye ground findings.

I know of no valid method of shedding light on this problem from my data. The interpretation of focal arteriolar changes known to be due to toxemia of pregnancy is complex. Like the significance of albuminuria or elevation of blood pressure, eye ground findings of the focal arteriolar type must be considered in the light of the entire clinical picture by the obstetrician.

There is evidence to indicate that when retinopathy is present changes are occurring which may result in intrauterine fetal death, and will likely cause postpartum hypertension. Wagener,[9] from studies of Schiötz and Masters, as well as from several cases of his own, indicates that when retinopathy occurs before the twenty-eighth week of pregnancy there is only a 25 per cent chance of obtaining a live baby and nearly 100 per cent chance of postpartum hypertension resulting if the pregnancy continues.

The absence of eye ground changes during the toxemia of pregnancy in question is significant but less so than in the positive sense. All eye ground changes observed during toxemia of pregnancy are not due to the disease in question. If the changes are known to be present before the toxemia (before the last trimester for example) and are static, there is then information that at least one segment of the vascular tree does not demonstrate evidence of a new disease process. The same is true when no eye ground changes occur at all. Interpreted in the light of other clinical and laboratory data, this information may be of value in the management of a patient with toxemia of pregnancy.

Aside from the above significance of the eye grounds in toxemia, one condition stands by itself. When detachment of the retina occurs during toxemia of pregnancy (and not of the idiopathic variety) it, in itself, is indication for termination of the pregnancy. Even though residual vascular damage does not always follow retinal detachment, the damage to the visual apparatus is too great to allow it to persist without substantial reason. The cases of Clapp[10] and those of Schiötz[11] are not conclusive of proving this point but a review of their cases points very strongly toward gross residual damage to the retina.

Summary and Conclusions

1. The fundi of one hundred patients with toxemia of pregnancy were studied and the findings tabulated.

2. Pathologic ophthalmoscopic findings were present in 27 per cent of the patients.

3. The findings are compared with those in other reports.

4. Eye ground changes due to toxemia of pregnancy have the following significance grouped according to severity. Here I use data of others as well as my own.

a. Retinal detachment is an indication for termination of the pregnancy.

b. Retinopathy before the twenty-eighth week of pregnancy is an indication in itself for termination of the pregnancy on a statistical basis.

c. Arteriolar changes alone mean that one part of the vascular tree is undergoing pathologic alteration. This direct evidence of disease in one part of the vascular tree must then be interpreted along with other indirect evidence of disease (such as urinalysis, blood pressure) by the obstetrician and the obstetrician alone.

5. In evaluation of arteriolar changes during toxemia of pregnancy, several observations must be made to determine the phase of the arteriolar disease process presented. This is of great importance.

6. The retinal changes more or less parallel the hypertension.

7. The retinal changes roughly increase with the age group studied.

8. Albuminuria, urea clearance, and uric acid clearance tests did not appear related to the incidence of fundus changes.

This study was done at the suggestion of the late Dr. James Norton. I wish to thank Drs. Samuel Cosgrove and Edward Waters for permitting me to see their patients. I also want to thank Drs. Gordon Bruce and Leon Chesley for helpful criticisms.

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POSTURAL SHOCK IN PREGNANCY*

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SHOCK is a well-recognized cause of maternal death and its occurrence in pregnancy, labor, or the puerperium calls for prompt diagnosis of the cause and equally prompt treatment to avoid fatality. This presentation is concerned with a form of shock not associated with any serious underlying disease, probably never fatal, which can possibly be spoken of as physiologic.

Circulatory collapse or primary shock in late pregnancy may be initiated or aggravated by change in position to the dorsal recumbent posture, and this shock may be relieved or treated by change from that position. This type of shock, occurring while the patient is lying down, and without apparent cause other than the patient's turning onto the back, is rare enough in any major degree that it has not impressed many observers. A severe case, such as the first reported here, is quite striking. Because of the interest aroused by this first case other cases were contributed during the year and form the basis for this paper.

It seems almost a universal custom to place shocked patients in the dorsal recumbent posture, yet in pregnant women this may be the worst possible position. In retrospect one notes how frequently women with premature separation of the placenta or those in hard labor insist upon lying on the side because it is less uncomfortable. Emptying the uterus changes this positional preference, and in the cases observed so far it removes the shock tendency produced by position alone. Such observations must have been made frequently, but have rarely been reported.[1] The following case histories are recorded.

CASE 1.—This 29-year-old gravida i, who showed no abnormalities in prenatal history or physical examination, was admitted with ten-minute pains, a blood pressure of 128/90, pulse 82. As the resident went in to see her she said, "I feel funny," and went into profound shock. She later said that she had just turned from her side to her back and suddenly "felt tingly and faint." The blood pressure was 0/0 and the heart rate slow. She was given 5 per cent dextrose intravenously, Pantopon ⅙ grain, and Coramine.

Twenty minutes later when I saw the patient she was semiconscious, white, and sweating profusely. She was put in an oxygen tent, plasma started, and the foot of the bed elevated. The blood pressure was now 60/0. Within one half hour the pressure rose to 110/70 with a pulse of 90.

Two hours after the initial episode the statement about turning had been elicited and one of my colleagues had remarked about seeing similar milder cases. At his suggestion the patient was turned to the side, shock blocks removed, and oxygen discontinued. On the side her pressure was 114/70 with a pulse of 84. In another two hours she was experimentally turned onto her back again. Within a minute the pressure fell to 82/70, 84/60, and 60/40, she again became pale, and the pulse slowed. She was immediately turned to her side and the pressure rose, with a pulse of 102.

*Read at the annual meeting of the Texas Association of Obstetricians and Gynecologists, Feb. 9, 1951.

The rest of her labor was carried out on the side with occasional pressure fluctuations during the day, once to 60/40 without apparent cause or symptoms. In general the pressure ranged around 110/60.

After eight hours of labor she was ready for delivery. The pressure was now 120/70. She was given a gas anesthetic while on her side and then turned to her back and delivered by outlet forceps of a male 7-pound infant, normal save for some skin peeling. One hour post partum the patient's pressure was 104/80, pulse 60. She had no further complications, and change in position caused no appreciable circulatory changes. Close questioning revealed that she had never had any trouble on her back save for the episode reported.

Comment.—In this case the change in position alone seemed to be the precipitating factor in shock. The patient had had no manipulation, no medication, and very little pain, any one of which might produce primary shock. Because of these facts, and particularly the severity and duration of the shock, this case was most arresting.

CASE 2.—This 23-year-old para i was admitted for induction one week from term with a cervix 2 cm. dilated, the head engaged, blood pressure 102/68, pulse 76. During the perineal preparation she felt faint and sweated profusely, but recovered when she sat up. Her physician ruptured the membranes, and, within a minute, while on her back, she went into shock. The blood pressure was 0/0, the patient pulseless and semiconscious. When she was turned to the side her pulse was felt within 30 seconds and the pressure was 90/60, rising to 100/75. She was willing to cooperate in an experimental study, and after full recovery turned to her back. The pulse did not accelerate, but became thinner as the pressure fell steadily over the next minute to 80/60, 74/55, and 45/30, at which point shock became imminent, the patient yawned, became pale, and asked to turn to her side. On her side the pulse became fuller and the pressure rose to 100/70.

At 5 cm. cervical dilatation she received sedation with Demerol-scopolamine. The pressure was 115/80. She was turned to her back, the pressure fell to 70/50, she began yawning, and asked to turn to her side, following which the pressure rose to 118/94.

Cyclopropane anesthesia was given and outlet forceps used to deliver a normal 7 pound, 6 ounce infant. The postpartum course was uneventful. On the day after delivery prolonged periods on her back produced no appreciable pressure changes, readings of 100/70 and 90/60 being obtained on the back and 95/76 on the side.

Comment.—This is another case of pure postural shock. The patient had had no manipulation when syncope first appeared. On the second occasion, following membrane rupture, it was almost certainly the position and not the procedure which produced the shock. In this patient the syndrome could be produced at will, but she was not sent into complete collapse. It is to be noted that it occurred only in late pregnancy, was relieved by turning to the side, and was completely cured by emptying of the uterus.

CASE 3.—This patient was a 26-year-old gravida i whose blood pressure range in pregnancy was from 110/60 to 130/70. In the last trimester she experienced shortness of breath while lying on her back, and if she persisted in this position there was numbness of the arms. On admission the blood pressure was 90/60 with a pulse of 76. When labor was well established she was given Demerol, 100 mg., which was repeated two hours later. In another three hours she was given Seconal, 3 grains, and hyoscine, $\frac{1}{100}$ grain. Vaginal examination showed the cervix thick and 6 cm. dilated, with the head in posterior position. She was given saddle block anesthesia with 2.5 mg. Heavy Nupercaine, and put on her back. Twenty minutes later, while on her back, the blood pressure dropped to 0/0 and the pulse was not perceptible. She did not lose consciousness. Intravenous fluids, ephedrine, and oxygen were given, and the pressure gradually rose to 60/? and then to 80/70, with a heart rate of 130. Turning the patient to her side was followed by an immediate rise in pressure to 130/70 and a fall in heart rate to 70. Later momentary turning to her back caused an acceleration of the pulse but she was not left in this position long enough to produce a fall in blood pressure. During the rest of labor the pressure ranged from 124/78 to 100/65.

Eight hours after the initial shock, with the saddle block completely worn off, she was given cyclopropane and a forceps rotation of the head was attempted. This failed, and as it was now obvious that delivery from below would be very difficult, she was moved to surgery for immediate cesarean section. The blood pressure had fallen to 80/60 during the anesthesia and the early operation, but upon delivery of the baby it was recorded at 110/88, and remained at this level during the rest of the operation. Post partum the patient had no difficulty in lying or sleeping on her back.

Comment.—In this case there were many factors that could have caused or contributed to the shock, the main one being anesthesia, the first spinal, the second general. In each case it required a relatively long period on the back before the pressure fell, but this was also true during her pregnancy. The fact remains that turning onto the side caused a marked rise in blood pressure and dramatic improvement in spite of the apparent cause of the vascular collapse, and that delivery produced complete and permanent relief.

CASE 4.—This patient was a 33-year-old Negro gravida i, moderately obese, and a known hypertensive. On her first prenatal clinic visit at 20 weeks' gestation, the blood pressure was 160/100. She was admitted to the hospital for study and found to have normal kidney function and only slight eye ground changes. On admission at term her blood pressure was taken both while she was on the side and on the back; on the side it was 144/112, on the back 118/98.

At full cervical dilatation, with the head on the pelvic floor, she was given saddle block anesthesia with 2.5 mg. Heavy Nupercaine. The blood pressure fell to 0/0, she began to sweat profusely, and the pulse was imperceptible. Ephedrine was given both intramuscularly and intravenously with no response. Oxygen and plasma were started with still no rise in blood pressure. At this point, twenty-five minutes after the initial shock, the patient was turned to her side and showed immediate improvement. Within two minutes the pressure was 160/100 and it went as high as 200/120. After it was stabilized she was again turned to the back and delivered by outlet forceps of a normal child. There was no further trouble.

Comment.—In this case the spinal or saddle block anesthesia obviously precipitated the circulatory collapse. There was failure to respond to ordinary therapy for shock until she turned to the side, and then response was immediate. It is freely admitted that it could have taken the administered vasopressors this long to act, and that the patient might have responded to them alone. But in the light of the previous cases, it seems more than coincidental that a marked and sudden improvement should have occurred after change in position.

CASE 5.—This 19-year-old gravida ii had had one spontaneous abortion. The current pregnancy was uneventful, with a blood pressure range of 134/74 to 124/64. On each office visit she had an abdominal examination and experienced no discomfort on her back until at 27 weeks she suddenly felt faint during an examination. A blood pressure of 30/0 was obtained. She was pulseless and pale, but not unconscious. When she was turned slightly to the side the pressure was 98/60 with a pulse of 60. There had been no previous attacks, and she had never fainted. She is still undelivered, and will be watched with interest.

This case is included because of the relative frequency with which this type is observed once one is aware of the syndrome.

CASE 6.—This patient discovered for herself the relationship of position to discomfort. She was a 34-year-old gravida iii whose first two pregnancies had been terminated by cesarean section. During the last trimesters of the second and of the current pregnancy she was unable to sleep on her back because it caused shortness of breath, nausea, and numbness of the hands.

She was scheduled for elective section near term. On the stretcher to the operating suite she lay on her back and by the time she reached surgery she felt faint and had to turn to her side. She moved onto the table and onto her back, felt sudden nausea, and the

pressure was found to be 30/0 with a barely perceptible pulse. She was given ephedrine and the pressure rose to 80/30. She was then turned to her side and given a spinal anesthetic. Immediately after delivery of the baby the patient's pressure rose to 140/68 and leveled off at 100/68. There was no further difficulty, either during operation or post partum.

Comment.—This patient demonstrates all of the significant points: the feeling of faintness when turned to the back, relieved by change of position; the fall of blood pressure that accompanies these symptoms; temporary relief obtained by turning; and the complete and immediate relief after emptying of the uterus.

Experimental Observations

In view of these cases, further investigations have been begun on the effect of change of position on the blood pressure of pregnant women at term. Only a small series has been recorded so far, certainly not enough to be of any statistical value, but several interesting observations have been made during the course of the study. A series of readings was taken with the patient on her back and on her side, allowing at least a minute for stabilization after the muscular effort of turning.

The first difficulty is in finding what is a significant variation in blood pressure. In thirty-six of the fifty cases there was a variation of ten or more points systolic in the various readings, or in 75 per cent. There was a variation of ten or more points diastolic in 30 cases, or 60 per cent. Therefore a ten-point variation in itself is a frequent occurrence. However, if these cases are broken down, we find the following:

There was a ten-point difference in the highest systolic reading on the side as compared to the highest systolic reading on the back in 13 cases, and of these cases the higher reading was on the side in 7 and on the back in 6. This is therefore of no significance. But there was a difference of 10 or more points systolic in the lowest reading on the side as compared to the lowest reading on the back in 15 cases, and in these the reading was higher on the back in two cases and on the side in 13 cases.

There was a difference of ten or more points diastolic in the highest reading on the side as compared to the highest reading on the back in 14 cases. Of these the reading was higher on the back in 5 cases and higher on the side in 9 cases. Of the 15 cases with a ten-point difference diastolic between the lowest reading on the side and the lowest reading on the back, the higher reading was on the back in 3 cases and on the side in 12 cases.

From these figures one may draw the inference that with the higher pressures there is little difference due to position, but that the lowest pressures will usually be found with the patient on the back. A continued study with a long series is needed to establish any definite pattern.

Several patients remarked that in late pregnancy they could not comfortably stay on the back because it produced a variety of symptoms—nausea, shortness of breath, faintness, or pain or numbness of the arms. However, in many cases it took perhaps half an hour for these symptoms to develop. Only one patient in the series showed significant blood pressure changes in the routine readings and later developed shock. This was Case 4, where shock followed spinal anesthesia. One other patient stated that she could not stay on her back because it made her feel faint. Her pressure on the side was 112/68. When turned to her back the pressure fell to 98/70 and 90/70 and the pulse became very rapid. She felt faint and refused to continue with the experiment. On her side again the pressure rose to 110/80 and the pulse, which had been about 150, fell to 86.

Comment

Bridgen, Howarth, and Sharpey-Schafer[1] show vasovagal fainting and changes in peripheral blood flow as a result of tilting, the lordotic posture, and spinal anesthesia to be the same as those in this syndrome in pregnancy, namely, a fall in blood pressure, a rise in inferior vena cava pressure, and a decrease in forearm blood flow. These writers observed one case quite identical with Cases 1 and 2.

Runge[2] observed in 1924 that venous pressure was higher in the legs than in the arms in late pregnancy. In studying changes during cesarean section, McLennan[3] noted a drop in femoral vein pressure to normal as soon as the baby was delivered, and believes that the presence of the fetal mass in utero is the major factor in maintaining venous pressure at abnormal levels. Bridgen, Howarth and Sharpey-Schafer[1] found that the leg vein pressure in a subject in late pregnancy rose 7.5 cm. in the supine position and fell on slight turning to the side. Women in early pregnancy showed no changes in forearm blood flow or in leg venous pressure with similar postural changes.

It has been postulated that in late pregnancy the uterus may obstruct the veins of the abdomen when the subject is in the strictly supine position, causing a rise in venous pressure caudally and a fall in the pressure in the right auricle. This amply explains the symptom complex, nausea, shortness of breath, faintness, sweating, the heart rate changes and fall in blood pressure being due to decreased cardiac output; pain and numbness of the arms must result from decrease in the forearm flow. But it does not explain why the syndrome does not appear in all patients, nor even always in the same patient.

Davis[4] calls this type of patient the "circulatory weakling" and cites as manifestations abnormal cardiac changes in response to change in position as well as the production of collapse in these susceptible individuals by various other stimuli.

The importance of these observations is that recognition of the syndrome may save much worry and unnecessary treatment.

Summary

1. The dorsal recumbent posture may produce discomfort or circulatory collapse in late pregnancy. Turning to the side will relieve this condition, as will emptying of the uterus.

2. These postural changes are apparently due to obstruction of the venous return from the pelvis and lower extremities by the pressure of the gravid uterus.

3. Shock from posture may be superimposed on shock from other causes.

4. Where there is a variation in blood pressure with change in position in late pregnancy, the lowest pressures will usually be found with the patient on the back.

5. In treating shock in pregnant women, it may be wise to have the patient on the side.

I wish to thank Dr. Herman L. Gardner for permission to report three of his private cases.

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Discussion

DR. M. J. MEYNIER, JR.—This very interesting paper presents the little-observed phenomenon of the signs and symptoms of shock in late pregnancy being diminished by a mere change in posture. The state of shock, thus alleviated, may be from mild to a threatening degree.

The more serious, pathologic types of shock, where the uterus has not been emptied, may, in some cases, be better controlled by recognition of the existence of postural shock.

Obstetrical patients are ideal for the making of such a study, since, in late pregnancy, with their increased blood volume and accompanying vasodilation, increased vasomotor and emotional instability, any manifestation of a shocklike reaction is accentuated.

In three of the cases reported, I feel that spinal anesthesia had a positive bearing on precipitating the patient's shock, though, in one case, the added major obstetrical procedure was also a contributing factor. It has been definitely demonstrated, however, that there was marked improvement in all the cases when the patient was turned on her side.

The observations in this paper, which includes three cases of saddle block, may give us a belated explanation of deaths from full-sized doses of various spinal anesthetics used in obstetrics ten to twenty years ago.

Since saddle block is given in smaller doses, usually sufficiently long before delivery to observe and treat untoward changes before delivery and to delay delivery until they are controlled, serious accidents are rare. But when we formerly used spinal anesthesia as a terminal anesthetic, usually for cesarean sections, even if the idea of postural advantage had been thought of, it could not have been used, as the incision had frequently already been made.

In the light of this present study, posture in some cases may have caused sufficient increase in the depth of shock to cause death.

DOUBLE SAC WITH SECONDARY RUPTURE OF THE BAG OF WATERS DURING LABOR. A CLINICAL ENTITY, AND ITS EXPLANATION FROM EXAMINATION OF THE MEMBRANES

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SINCE the beginning of modern scientific obstetrics, physicians have been puzzled by the clinical phenomenon of the bag of waters of a single pregnancy rupturing twice. In some instances, the initial rupture of the sac occurs many weeks before the onset of labor, in which case the physician explains it as a "high rupture" that has sealed itself off to allow pregnancy to continue. Such explanations have very little scientific basis, but are accepted for want of a better one. DeLee states in his textbook in the chapter on the physiology of labor: "The Rupture may take place high up, and the waters dribble away at each pain." As all clinicians know, there are a number of variations in the time, manner, and amount of the rupturing of the fetal membranes, but in this report the author is concerned only with those cases in which there is unquestionable evidence of the rupture of the membranes prior to, or at the beginning of labor, followed by the appearance of an intact sac containing fluid at the end of labor.

Clinical Material

Altogether there were 16 cases personally observed by the author. All degrees of parity are represented. The longest interval between rupture of the first sac and that of the second was 15 days. The shortest interval was a few minutes. In all cases, the first sac ruptured spontaneously and the second sac was punctured artificially. In every case, verification of rupture of the membranes initially was made by house officer or nurse, and confirmation of the presence of the intact second sac (before puncture) was made by other staff members present in the labor suite and by house officers and nurses. In many of the cases, by meticulous examination of the expelled membranes and placenta, it was possible to demonstrate the complete separation of the amnion from the chorion and/or the retraction of the chorion away from the opening in the amnion. Special care was taken to deliver the placenta and membranes with the least amount of force or trauma.

Case Reports*

CASE 1.—H. G., gravida ii, aged 25 years, had a history of one previous pregnancy, characterized by premature rupture of membranes at 8 months' gestation and the onset of labor two weeks later, resulting in the birth of a live child, weight 5 pounds, 2 ounces (June, 1943). She was first seen by the author at the beginning of her second pregnancy, last menstrual period, Aug. 20, 1944, estimated date of confinement, May 27, 1945. On

*To prevent repetition of similar details and to save space, only four of the 16 cases are described in this report.

May 16, 1945, she reported that the membranes ruptured at home in bed. There was a constant escape of fluid for several days, and the patient observed that this was a repetition of what occurred in her first pregnancy. On May 27, twelve days after the initial escape of fluid, labor pains began, and she was admitted to the Sinai Hospital at 6:30 P.M. of that day. Six hours later, the cervix was fully dilated. She was prepared for delivery, and on vaginal examination an intact sac of membranes was first palpated and then visualized. The sac was tense, and was of a bluish-green hue, the color being more vivid than usual in an unruptured bag of waters. The sac was punctured at 12:45 A.M., a considerable amount of fluid escaped under moderate pressure, and the baby (5 pounds, 8 ounces) was delivered spontaneously five minutes later. The membranes were very carefully examined following delivery. The striking thing about their appearance was the manner in which the outside layer (the chorion) had retracted toward the placenta (Fig. 2). That finding was entirely compatible with the history of an interval of 12 days between the two ruptures, during which interval the edges of the ruptured chorion withdrew higher and higher from the internal os toward the margin of the placenta.

CASE 2.—C. S., gravida i, aged 20 years, estimated date of confinement, Nov. 14, 1947, had a normal prenatal course. Labor began on Sept. 24 at 2 A.M. She was admitted to Sinai Hospital at 4:45 A.M. in premature labor, membranes intact. At 5:20 A.M., the membranes ruptured spontaneously with escape of from 350 to 500 c.c. of fluid. Examination immediately afterward revealed the cervix fully dilated, but the presenting part could not be identified because it was preceded by a cystic mass. This mass began to protrude through the outlet, and it was punctured. Clear fluid shot out in a stream under pressure. The baby (premature) was delivered spontaneously immediately afterward. The placenta was retained and was removed manually. Because of the manual removal, examination of the membranes for evidence of separation of the chorion from the amnion was not carried out. In this case, the interval between ruptures was unusually short, merely a matter of several minutes. This is the only case out of the sixteen in which rupture of the two sacs followed in quick succession.

CASE 3.—C. N., gravida i., aged 23 years, last menstrual period Feb. 27, 1947, estimated date of confinement Dec. 4. Pregnancy was characterized by severe hyperemesis. On Jan. 4, 1948, at 11:30 P.M. the patient's water broke and she was admitted to Sinai Hospital two hours later. The escape of appreciable amounts of fluid on admission and for a number of hours subsequently was verified by several nurses and interns in attendance. The patient went into labor the same morning, but the first stage was characterized by uterine inertia, labor coming to a complete standstill at 5 cm. dilatation. At 9:30 P.M., a vaginal examination was done, and an intact sac of membranes found. The sac was punctured, fluid in moderate quantity escaped, and labor progressed very satisfactorily from then on. At 12:15 A.M. (less than three hours later) the cervix was fully dilated, and at 1:02 A.M. patient was delivered of a live male child by low forceps and episiotomy. The third stage was normal. In this case, 22 hours elapsed between the initial rupture and the puncturing of the intact sac. Inspection of the membranes revealed clear-cut separation of the amnion from the chorion, with the amnion collapsed around the umbilical cord.

CASE 4.—P. P., gravida i, aged 27 years, last menstrual period April 27, 1950, estimated date of confinement Feb. 3, 1951, had an uneventful prenatal course. She had premonitory labor on January 27 and 28, for which she was admitted to Sinai Hospital and discharged. She was home only two hours when she reported that her water had broken and that she was returning to the hospital immediately. The author was present at the time of her second admission, and the patient presented the typical picture of the excited nullipara walking into the maternity division with her hand between her thighs and the water trailing behind her. This was a 6:00 P.M. Active labor began the following morning after midnight, and by 8:30 A.M. the cervix was fully dilated. The second stage was prolonged because the head

would recede after each pain. The position of the suture and the fontanelles was clearly defined by rectal examinations as left occipitoanterior, and there was no explanation for the failure of descent of the head to the perineum. The patient was prepared for delivery, and vaginal examination revealed an intact sac by both palpation and inspection. The sac was punctured. In this case, the sac was not tense, and a very small amount of fluid escaped. Delivery of a full-term child was effected by low forceps and episiotomy. Examination of the membranes revealed the amnion completely peeled away from the chorion and lying collapsed around the placental end of the umbilical cord. In this case, 18 hours had elapsed between the initial rupture and the artificial rupture prior to delivery.

Comment

All physicians and midwives are familiar with the phenomenon of the "caul," or the unruptured sac covering the baby's head as it is born. This may be explained by the fact that the chorion ruptures and the unruptured amnion herniates through, as it were, and thus comes to cover the infant's head while passing through the vulva. In like manner, we sometimes see a pouch of membranes partially filled with fluid appear through an incompletely dilated cervix. This may also be caused by the rupture of the outer layer (chorion), with the amnion herniating as a sac. These well-known clinical variations in the presentation of the fetal membranes do not occasion very much speculation by the attendant. In cases of early or premature rupture of the membranes, followed in many hours or several days or even longer by the formation of a definite bag of waters which ruptures spontaneously or artificially at the end of labor, a similar process but with manifestations different from the previously mentioned clinical varieties takes place. These are the cases which evoke surprise and speculation on the part of the attending physician, not because they are rare, but because two separate and distinct ruptures of a "single" bag of waters is mystifying. What is the explanation?

The single point in question to be raised in the acceptance of the author's explanation is the presence of fluid between the two layers of the fetal sac, the amnion and the chorion laeve. In other words, one must accept the premise that liquor amnii can be present outside the amniotic membrane. Starting with the widely held theories as to the origin of the amniotic fluid, namely, by transudation from the maternal circulation and by secretion from the amniotic epithelium, it is necessary to include the possibility of the appearance of the fluid on the chorionic side of the amniotic membrane. The amnion being a thin, single layer of epithelium, there is much plausibility to the view that by transudation or secretion, amniotic fluid can pass into the space between the amnion and chorion, converting it into an actual cavity containing fluid. DeLee states: "Sometimes an accumulation of fluid between the two membranes occurs, and the chorion ruptures, while the amnion remains intact. Thus there seem to be two bags of water." In his textbook description of the membranes, DeLee pictures the chorion, or outer layer, as thick, cloudy, somewhat opaque, and *easily torn,* whereas the amnion is transparent and *tougher.*

There is currently a great interest as to the pathogenesis of amniotic fluid embolism. In an effort to throw some light on the manner in which amniotic fluid enters the maternal circulation, Leary and Hertig[4] studied 14 placentas from cases in which there was no maternal morbidity. Each of these placentas showed the presence of amniotic squamous cells in abnormal locations, and 10 of the 14 placentas had squamous cells between the amnion and chorion. This is further proof that the amniotic membrane is permeable to the contents of the amniotic sac.

With the above facts in mind and referring to the accompanying diagrams, the sequence of events in double rupture of the membranes becomes clear. As the fluid accumulates in the chorio-amniotic space, the pressure therein increases. The weakest spot in the chorion, just above the internal os, where erosion is most likely to occur, gives way to the pressure of the fluid above it, and the chorion ruptures with the escape of whatever fluid is present. As soon as the rupture occurs, the edges of the torn chorion retract

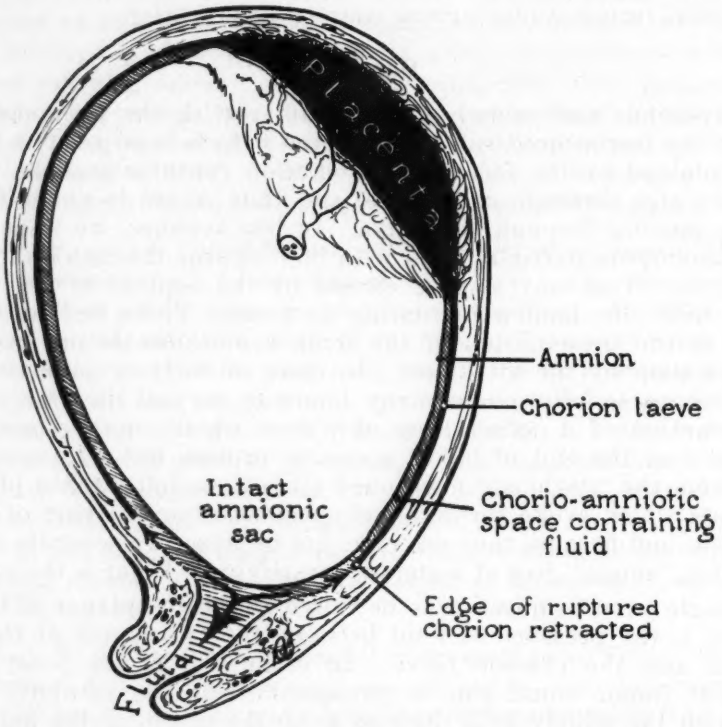

Fig. 1.—Diagram showing space between chorion and amnion containing fluid, mechanism of ruptured chorion (leaving amnion intact), and retraction of the edge of chorion away from the internal os.

away from the internal os, and, if very much time elapses before labor ensues, it is conceivable that the edge of the chorion may retract high up in the uterine cavity, converting the chorion into a shrivelled membrane suspended from the placental margin. (This is not to be confused with extramembranous pregnancy, reports of which were recently made by Baker and Savage,[3] and previously by Siddall.[2]) In this way, the amnion can come to lie directly next to the decidua vera for a variable distance between the internal os and the placenta. Whether the chorion retracts for some distance or not has no bearing on the rest of the mechanism of the phenomenon. The naked amnion now is exposed to the margin of the cervix, and as the cervix dilates, the sac which presents in front of the baby's head is made up of amnion alone. This sac has its own content of fluid and its own hydrostatic pressure, and depending on these factors the sac will remain intact until ruptured by the forces of labor or by artificial means. In practically every case in this series, it was necessary to puncture the sac with a sharp instrument.

While it is obviously impossible to measure the amount of fluid escaping, some effort was made to compare the amounts in the two sacs. There was

no constant relation between the amounts, that is, neither the first sac nor the second one contained a greater amount, and thus no factor in the hydrostatic pressures of the two sacs could be assumed or hypothecated. In some cases, the amount of fluid escaping at the original rupture was large, and that of the second rupture small. In other cases, the reverse was true. In still others, the relative amounts were roughly equal. There were no cases of polyhydramnios in the series.

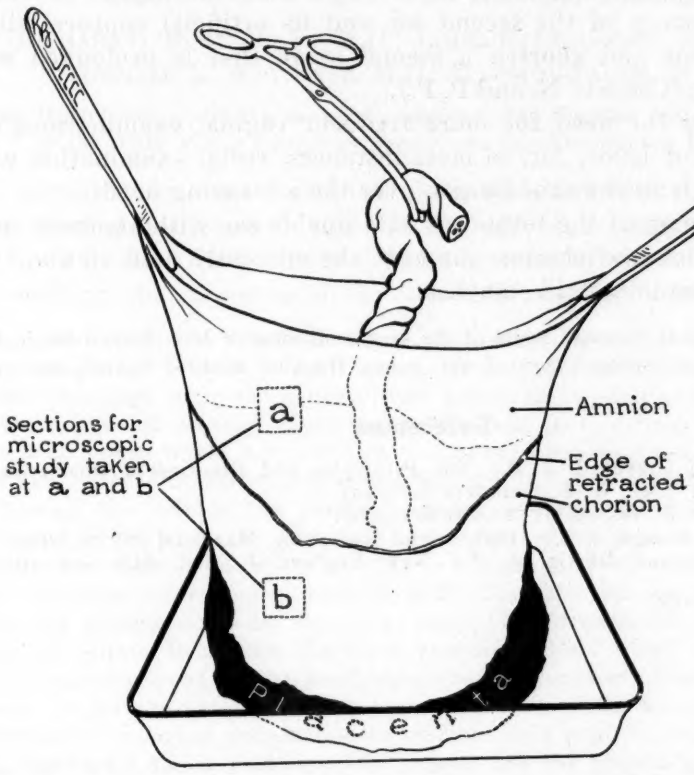

Fig. 2.—Examination of the membranes following delivery showing chorion retracted from the recently punctured opening in the amniotic sac.

Conclusions

Based on 16 personally observed cases, of which four are reported in detail here, including minute examination of the membranes following delivery, the conclusion is reached that double sac with secondary rupture of the membranes in a single pregnancy occurs with a definite but undetermined frequency, sufficiently often to warrant the attention of the obstetrician.

The explanation for the phenomenon, namely, the presence of a volume of fluid between the amnion and the chorion, is consistent with the facts now known concerning the physiology of pregnancy and labor.

Acceptance of this new clinical entity should serve to allocate "high rupture" of the membranes to a place of discarded obstetrical lore.

Double sac of membranes can explain an unusually long latent period following premature rupture of the outer sac (Case H. G.).

It can serve as an explanation for the apparent immunity to infection of both mother and infant following long periods with "ruptured membranes."

It may explain an occasional failure to induce labor by means of artificial rupture of the bag of waters, that is, where an "amniotomy" is performed on the *chorion* alone.

Clinically, recognition of the possibility of a double sac can be of real value, because the discovery of the second sac and its artificial rupture will most likely hasten labor and shorten a second stage that is prolonged without other explanation (Cases C. N. and P. P.).

It emphasizes the need for more frequent vaginal examinations during the second stage of labor, for, in most instances, rectal examination will not reveal the presence of the thin amnion over the advancing head.

The phenomenon of the formation of a double sac with amniotic contents between the amnion and chorion supports the currently held views as to the pathogenesis of amniotic fluid embolism.

Acknowledgment is herewith made of the kind assistance of Miss Ranice Birch, Director of the Department of Medical Art of the Johns Hopkins Medical School, who executed the above drawings.

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CEREBRAL VENOUS THROMBOSIS IN THE PUERPERIUM

Report of Two Cases With Necropsy Findings

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THE subject of puerperal cerebral thrombosis has received but little comment from obstetricians in this country, although a number of reports are to be found in the British literature.[2-7] Because of the unusual occurrence of this accident, the recording of the following two cases may be of interest.

CASE 1.—(NCBH No. 117629.) The patient, a 31-year-old, white, para vi, was delivered spontaneously with an occiput anterior of a normal term infant under drop ether anesthesia. Although labor and delivery were unremarkable, uterine hemorrhage amounting to 600 to 800 ml. occurred approximately one hour post partum. Blood pressure was maintained at normal levels, however, and the patient received 500 ml. whole blood. The enlarged and softened uterus responded satisfactorily to oxytocic administration.

Following this episode, the patient appeared well and was asymptomatic until 15 hours after delivery when she complained of severe, sharp pain in the left flank that radiated anteriorly across the abdomen. Thirty minutes later she exhibited signs of shock and the blood pressure fell precipitously to 40/0. The pulse was unobtainable. Antishock measures and parenteral fluids, including whole blood transfusions, were administered promptly and within 45 minutes the blood pressure had stabilized at 105-120/50-60, but the patient had developed a right hemiplegia, and was confused, somewhat stuporous, and incoherent. A positive Babinski sign and sustained ankle clonus were present on the right side. Further neurological examination showed the right pupil to be larger than the left. Minimal right-sided facial weakness was present, and the patient experienced some impairment of deglutition. The deep tendon reflexes were hyperactive on the right. No aphasia was apparent (the patient was left-handed) although enunciation of words was somewhat awkward.

Concomitant with the onset of shock, a firm, extremely tender and rapidly enlarging mass, arising from the pelvis and almost entirely filling the left flank was demonstrated. This was believed to represent a hematoma of the broad ligament and retroperitoneal space. A diagnosis of cerebral thrombosis secondary to acute blood loss, shock, and anoxia was made, and in addition to oxygen administration, the patient was given 60 mg. of papaverine in hourly doses.

Gradual clinical improvement was apparent during the eleven-day period following the acute episode. The patient's sensorium became somewhat clearer, although she was easily confused and emotionally unstable at times. The mass described in the left flank decreased slightly in size during this period. Improvement in deglutition was noted and incontinence of feces, present initially, diminished. Papaverine medication was discontinued after six days. A lumbar puncture performed on the seventh postpartum day showed the cerebrospinal fluid pressure to be equivalent to 220 mm. of water with normal dynamics. Microscopic examination showed one erythrocyte and one lymphocyte per cubic millimeter. Cerebrospinal fluid glucose, protein, and chloride concentrations were within normal limits. No organisms were demonstrated by bacteriological culture.

The interim period of clinical improvement was terminated abruptly on the twelfth postpartum day by the onset of a series of Jacksonian convulsive seizures involving the face and extremities on the left. An electroencephalograph recorded during one convulsive episode showed a spike focus in the *left* temporal area. Neurological examination disclosed a positive Babinski sign and ankle clonus bilaterally. The deep tendon reflexes were increased on the right as previously noted. The right hemiplegia remained. Examination of the optic fundi showed venous engorgement only.

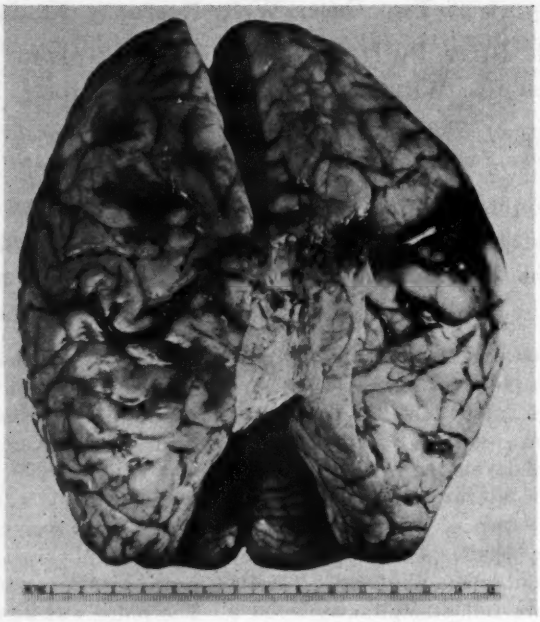

Fig. 1.—Brain of Case 1. Thrombosis of cerebral veins is clearly shown. On the surface of the left hemisphere can be seen irregular areas of petechial hemorrhage.

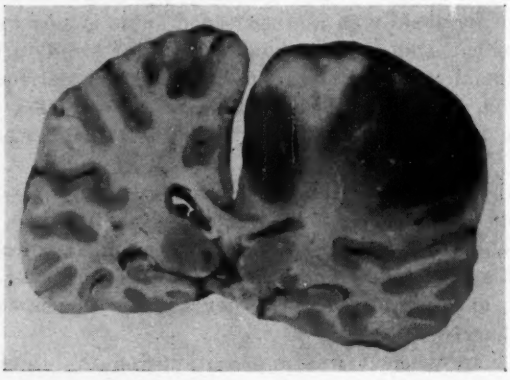

Fig. 2.—Brain of Case 1. Frontal section of specimen shown in Fig. 1 taken in the region of the Rolandic area. Note extensive areas of hemorrhage and necrosis.

Although extension of a venous thrombosis with sagittal sinus involvement was felt to represent the most likely diagnosis, in consideration of the patient's rapid mental deterioration, ventriculography, with normal findings, was performed on the fourteenth postpartum day, thus excluding the possibility of a mass lesion. Convulsions were controlled terminally by barbiturate medication, and with deepening coma the patient was maintained on parenteral fluids and gavage feeding. She died on the eighteenth postpartum day.

Postmortem examination showed thrombosis of three superior cerebral veins in the region of the pre- and postcentral gyri. Two large vessels on the right and one on the left were affected, the process extending to, but not involving the superior sagittal sinus. Scattered petechial hemorrhages were present in the left cerebral cortex, while in the right hemisphere areas of petechial and gross hemorrhage and encephalomalacia surrounded the deep extensions of the thrombosed vessels (Figs. 1, 2).

A number of thrombosed varicose veins were seen in the broad ligaments. In one of these on the left a ruptured aneurysmal dilatation was present. This defect was apparently the source of a large retroperitoneal hematoma that extended upward beneath the descending colon, involved the mesentery of the small bowel, and covered the pancreas.

This case is somewhat unusual in that the venous thrombosis developed in association with hemorrhagic shock on the day of delivery. Although clinical improvement was apparent after the initial accident, extension of the process resulted in the patient's death. As arterial thrombosis could not be definitely excluded at first as a diagnostic possibility, papaverine was administered in an effort to control spasm. It is of interest that convulsive seizures did not develop until late in the course of this patient's illness when extensive destruction of the brain occurred.

CASE 2.*—This 23-year-old, white, para ii, was delivered of a viable female infant at term from left occiput posterior position by Scanzoni's maneuver under nitrous oxide-oxygen anesthesia. Her prenatal course had been unremarkable.

Following delivery the patient was asymptomatic, ambulatory, and apparently well until the eighth postpartum day when she first complained of headache and it was noted that she was somewhat confused and mildly disoriented. Approximately four hours later she suddenly had a severe tonic convulsion. Examination showed generalized hyperreflexia, widely dilated pupils with the eyes deviated to the right. The eye grounds were normal. Babinski signs were negative and no clonus was demonstrated. The blood pressure was 150/90 and the urine gave a one plus test for albumin. It was assumed that the patient was an "atypical eclamptic" and she was given sedation with barbiturates, Pantopon, and magnesium sulfate. She had seven convulsions during the two-hour period after onset, the seizures being finally controlled by intravenous Pentothal Sodium.

With the onset of convulsions the patient became semicomatose, but her sensorium cleared somewhat after forty-eight hours at which time it was felt that she exhibited a sensory aphasia. No localizing neurological signs were apparent, however.

Lumbar puncture was performed on the ninth postpartum day (twenty-four hours after onset). The cerebrospinal fluid pressure was equivalent to 300 mm. of water and exhibited normal dynamics. The fluid had a pinkish tinge and contained 5,000 erythrocytes per cubic millimeter with many crenated cells. The Pandy reaction was one plus and the protein concentration was found to be 91 mg. per cent.

With deepening coma on the thirteenth postpartum day (five days after onset) lumbar puncture was repeated. The spinal fluid was xanthochromic and the pressure was equivalent to 280 mm. of water. The erythrocyte count was 30,000 cells per cubic millimeter. The patient became increasingly moribund and died on the fourteenth postpartum day, six days after the onset of neurological signs.

At autopsy a partially organized thrombus was demonstrated in the superior sagittal sinus. This process had extended into several of the superior cerebral veins of the left hemisphere resulting in an area of ischemia and necrosis in the left temporal lobe. The postmortem findings were otherwise unremarkable, and extracerebral sites of thrombosis were not found.

The clinical features of this case are fairly representative of primary venous thrombosis with sagittal sinus involvement. Consistent with the latter

*The authors are indebted to Dr. C. N. Burton and Dr. George Macatee, Jr., Asheville, N. C., for their kind permission to report this case.

diagnosis are the changes found in the cerebrospinal fluid. The incidental hypertension and albuminuria perhaps were related to the convulsive state of this patient. Papilledema might well have been demonstrated by repeated examination of the optic fundi.

Comment

Occasional reports of cerebral venous thrombosis during the puerperium have appeared in the literature for more than a century (for review see Refs. 1, 2). During the past fifteen years the clinical and pathological features of this condition have been re-emphasized in a number of reports[2-7] and the pertinent literature has been recently summarized by Hyland.[8] In spite of the fact that this complication has been recognized by physicians for many years, the total number of cases reported remains small, and its actual incidence is difficult to assess. Most authors, however, regard it as a most uncommon puerperal accident.

Briefly the typical case may be characterized clinically as follows: After a normal prenatal course, uncomplicated delivery, and apparently normal early postpartum period, weakness or paralysis rather suddenly develops, frequently in association with convulsive seizures which may be Jacksonian in type. The time of onset is usually within the first three weeks postpartum, although longer intervals have been recorded.[5, 7] Headache and confusion may precede the occurrence of frank neurological signs. As might be expected, the neurological manifestations are quite variable and are dependent upon the location, extent, and degree of brain damage, although Martin and Sheehan[5] have commented on the almost universal occurrence of convulsions even without involvement of the motor cortex. The paralysis may manifest itself as a mono- or hemiplegia and contralateral limb involvement has been reported.[2, 8] Aphasia and peripheral sensory disturbances are common. The cerebrospinal fluid pressure is typically increased with involvement of the superior sagittal sinus in which case papilledema is usually demonstrable. With significant meningeal or cortical bleeding, the spinal fluid will show the presence of erythrocytes, but is chemically unremarkable except for small increments in protein concentration in some cases.[2, 4, 5, 7, 8] Although adequate statistics are unavailable, the mortality has been estimated from 30 to 56 per cent.[2, 7]

A number of authors[2, 4, 5, 7, 8] have indicated that the clinical features of this condition are sufficiently unique to permit diagnosis during life, and in a small number of cases in which recovery occurred the diagnosis has been confirmed by exploration[5] or autopsy[5, 8] following death by other causes. Many cases undoubtedly pursue a benign course as may become apparent with increased clinical recognition and diagnosis.

The specific obstetrical problem is one of differentiating these cases from late eclampsia. Martin and Sheehan's[5] Case 2 in which coexistent hypertension and albuminuria were present, but with cerebral venous thrombosis demonstrated at necropsy, is representative of the problem in diagnosis that may be encountered in the early puerperium. The similar symptomatology of these two conditions increases the difficulty in reaching a decision. However, when the onset of symptoms occurs later than four days postpartum, eclampsia probably need not be given serious consideration. Hypertension with edema and/or albuminuria antecedent to the development of neurological symptoms is obviously of great differential diagnostic value in the immediate postpartum period.

The possibility of space-occupying intracranial lesions, epilepsy, or meningeal infection must be included in the differential diagnosis. The case history, together with clinical laboratory findings, should resolve the diagnosis

in most instances. Arterial thrombosis is generally more abrupt in onset, and recovery less complete than with venous thrombosis, although neurological residue may persist following the latter.[5] Arterial embolism is unlikely in the absence of organic heart disease, and its occurrence otherwise requires an opening between the right and left sides of the heart such as a patent foramen ovale.

The etiology of cerebral venous thrombosis in the puerperium remains obscure. It is considered as "primary" in distinction to thrombosis occurring with extension of infectious processes about the skull. Of interest is the fact that concomitant thrombosis is frequently found elsewhere in the body.[5, 8] Martin,[6] on the basis of Batson's[9] studies has suggested that the intracranial process is initiated by venous emboli derived from the pelvic veins and reaching the cerebral circulation through the vertebral venous plexus. Such a mechanism is considered unlikely by Kendall,[2] who believes the thrombosis to result from changes in the blood of puerperal patients that facilitate clot formation together with local damage to the cerebral vessels presumably occurring in labor. Although these opinions are of considerable theoretical interest, it would appear that a final decision in regard to etiology must await further experimental and clinical data.

Treatment has been critically evaluated by Hyland,[8] with whom we are in agreement in urging caution in the use of anticoagulant therapy on the basis that increase in cerebral bleeding at the site of thrombosis as well as uterine hemorrhage may result. Barbiturate medication is satisfactory for control of convulsive seizures, but morphine is contraindicated because of its depressant effect on the vital centers, particularly with increasing intracranial pressure. In the latter circumstance, with sagittal sinus involvement, dehydration procedures may be tried (concentrated serum albumin, hypertonic glucose) but repeated lumbar punctures[2] and careful withdrawal of cerebrospinal fluid is a more certain technique for the reduction of intracranial pressure. Supportive therapy including attention to fluid, electrolytes, and nutritive needs with good nursing care and the institution of physiotherapy as early as practicable need no comment.

Summary

1. Two cases of primary cerebral venous thrombosis in the puerperium are reported.

2. The clinical features and treatment of this condition are briefly reviewed.

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THE EFFECT OF AMPUTATION OF THE CERVIX UTERI UPON SUBSEQUENT PARTURITION*

A Preliminary Report of Seven Cases

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AMPUTATION of the cervix uteri in a young woman may have any or all of three effects upon her future childbearing: a reduction in the incidence of conception; an increase in the incidence of abortion and premature labor; a marked increase in complications attendant upon labor, with resultant increase in the operative delivery rate.

This is stated by Bonney[1] in effect: "Complete or almost complete removal of the cervix certainly lessens the probability of conception, and creates in the event of pregnancy, a marked tendency to premature emptying of the uterus." Titus[2] warns that "cervical amputation is still another cause for cervical stenosis and . . . deep lacerations attend the sudden rupture of stenotic cervices during labor, and once such a laceration starts, there is no certainty about its limitation."

In this preliminary study we have collected for analysis seven cases of parturition subsequent to amputation of the cervix. Two of these are presented as case reports.

Leonard[3] in 1914 analyzed 167 cases of amputation of the cervix. Seventy-two of these patients were married women in the childbearing years. Among this group he reported a subsequent conception rate of 19.4 per cent, of whom only 45 per cent carried to term. In support of the Emmet trachelorrhaphy, he collected 39 cases in which such a procedure had been performed in married women in the reproductive era. In this group the conception rate was 38 per cent, of whom 72 per cent carried to term.

Sturmdorf,[4] two years later, quoted extensively from Leonard's paper to emphasize the ill effects of cervical amputation upon subsequent pregnancy and parturition. He did not advocate the Emmet operation, however, being of the opinion that on "physiological, pathological, clinical, and technical grounds" trachelorrhaphy was not "efficacious as a curative measure." In his paper he reconciles these conflicting opinions by proposing a cervical operative procedure characterized by the preservation of the peripheral muscle fibers, in an attempt to accomplish the efficacy of cure of amputation without its untoward effects upon future childbearing. In this study we have not considered the Sturmdorf procedure to be an amputation of the cervix. It should be emphasized that in none of the cases reported herein has the operation devised by Sturmdorf been performed.

More recently the advocates of the Manchester operation, including Shaw,[5] Maier and Thudium,[6] and Gordon,[7] share the opinion that amputation of the cervix performed in conjunction with this operation has little effect upon subsequent parturition. Shaw states that "the operation is not a cause

*Read before the Baltimore Obstetrical and Gynecological Society, April 12, 1951.

of trouble in subsequent labors.'' Maier and Thudium report 13 full-term children and one abortion in 47 women on whom the Manchester operation had been performed. Of the twelve women reporting subsequent labors, the cervix had been amputated in ten cases. Gordon, while reporting good results regarding pregnancy subsequent to the Manchester operation with amputation of the cervix, retrenches however, and in his own practice does not include the latter procedure in his surgery on women in the reproductive era.

The innocuity of removing the cervix along with the Manchester procedure does not enjoy undisputed support, however, even among the British. Hunter[8] has collected and reported a series of cases of repeated abortion and a series of dystocia cases following removal of the cervix, with the result that he has proposed conservation of the cervix in operations for prolapse. He even suggests an operative procedure wherein the vaginal attachment of the cervix is advanced nearer the external os, effecting a relative shortening of the cervix by shortening its vaginal portion. Williams[9] reports an incidence of 49 per cent abortion and 19 per cent premature labor, for a combined total of 68 per cent, following amputation of the cervix.

Material

We have made no attempt to determine the effect of this procedure upon the subsequent rate of conception, a very large number of appropriately cross-filed cases being required necessarily to be of any statistical significance. The fact that, of roughly 30,000 obstetrical cases reviewed, only seven cases of pregnancy progressing to the third trimester following such a procedure have been uncovered, may in itself be of significance. Either these women do not conceive so readily or, if fertile, abort. Many of these abortions are not, moreover, recognized because they occur at home. In the seven abortions following amputation in our series, only one was a hospital admission case. The other six were uncovered during admission for complications in subsequent pregnancies.

Following amputation of the cervix there is a decrease in fetal salvage. As summarized in Table I, these seven women presented 23 pregnancies before operation. These pregnancies resulted in 21 full-term living normal children, one nonsurviving premature baby, and one early abortion, for an incidence of 91 per cent successful pregnancies. The early abortion in this series occurred in a patient five months following a major surgical procedure.

Following amputation of the cervix, these same seven women conceived a total of 14 times, resulting in only 3 full-term living normal children; 4 premature babies, none of whom survived; and 7 abortions, for an incidence of 21.5 per cent successful pregnancies. The average age of these women at the time they were subjected to this surgical procedure was slightly over 30 years.

Following amputation of the cervix there is an increase in the operative delivery rate. Prior to surgery these seven women had 22 pregnancies progressing to the stage of parturition, all 22 delivering by the vaginal route. Following operation, however, of the 7 pregnancies which progressed to parturition, there were 4 abdominal deliveries for an incidence of cesarean section of 57 per cent (Table II).

Following amputation of the cervix there are increased complications in those who deliver vaginally. All three vaginal deliveries evidenced either a prolonged first stage, or an increased latent period between rupture of the membranes and the inauguration of labor. The results of these deliveries were either stillborn babies or first-day neonatal deaths (Table III).

TABLE I

PATIENT	BEFORE AMPUTATION OF THE CERVIX			AGE AT TIME OF OPERATION (YEARS)	AGE AT FIRST SUBSEQUENT CONCEPTION (YEARS)	AFTER AMPUTATION OF CERVIX		
	FULL-TERM LIVING CHILD	PREMATURE LABOR	ABORTION			FULL-TERM LIVING CHILD	PREMATURE LABOR	ABORTION
1. J. W.	3	0	1	23	24	0	1 (stillborn)	3
2. E. D.	5	0	0	26	30	0	1 (lived 10 hours, 30 minutes)	0
3. S. D.	1	1 (lived 22 hours)	0	38	39	0	1 (lived 14 hours, 22 minutes)	0
4. G. J.	1	0	0	33	43	1 (section)	0	0
5. S. S.	1	0	0	28	29	1 (section)	0	2
6. A. F.	7	0	0	37	39	1 (section)	0	0
7. S. C.	3	0	0	29	30	0	1 (section lived 6 hours 2 minutes)	2
Total	21	1 dead 0 living	1	*Average Age* 30 years, 7 months	*Average Age* 33 years, 5 months	3	4 dead 0 living	7

TABLE II

PATIENT	OPERATION	RESULT
1. G. J.	Classical section	3,657-gram living normal child
2. S. S.	Elective low cervical section	2,977-gram living normal child
3. A. F.	Elective classical section	3,246-gram living normal child
4. S. C.	Classical section	1,531-gram child, lived 6 hours

TABLE III

PATIENT	LENGTH OF TIME MEMBRANES RUPTURED BEFORE LABOR	LENGTH OF FIRST STAGE	RESULT OF LABOR
1. S. D.	40 hours	6 hours, 43 minutes	1,616-gram baby, lived 14 hours
2. E. D.	193 hours	22 hours, 25 minutes	1,559-gram baby, stillborn
3. J. W.	2 hours	26 hours	567-gram baby, lived 10 hours, 30 minutes

Case Reports

CASE 1.—J. W., a 27-year-old white housewife, was admitted Aug. 2, 1950, from our obstetrical dispensary where she had been followed since June 27, 1950, her estimated date of confinement being Oct. 25, 1950. Her past history showed a 2,090-gram normal infant born in January, 1941, and a 2,637-gram normal infant in October, 1942. In October, 1944, at the age of 21 years, she had a modified Gilliam suspension of the uterus with plication of the uterosacral ligaments and appendectomy. In March, 1945, five months postoperatively, she aborted at 16 weeks. In May of 1946 she gave birth to a 3,317-gram normal child following an uneventful pregnancy.

One year following delivery, in June, 1947, she re-entered the hospital where her first operation had been performed, this time complaining of left lower quadrant pain of several years' duration. In her preoperative work-up the only mention of the cervix uteri is found as part of a routine pelvic examination, this organ being described as firm, lacerated, freely movable, and in good position. There was no mention of the cervix in the preoperative diagnosis. At this time, at the age of 23 years, she had a repair of a rectocele, amputation of the cervix, and presacral neurectomy. Since this operation she had aborted three times at 16 to 22 weeks of gestation.

She was admitted to the hospital two hours following spontaneous rupture of the membranes at home, complaining of mild cramps. Following a 26-hour first stage, she delivered spontaneously from frank breech presentation a 567-gram fetus who lived 10 hours, 30 minutes.

CASE 2.—E. D., a 30-year-old white housewife, was admitted Aug. 11, 1950, from our obstetrical dispensary where she had been followed since June 20, 1950, her estimated date of confinement being Jan. 13, 1951. Her past history related five full-term normal deliveries in 1938, 1940, 1941, 1942, and 1944. Two years following delivery of her last child she was admitted to the hospital complaining of profuse vaginal discharge of two years' duration, white and creamy in character, blood-tinged upon occasion.

Her menstrual history was irregular but had been so since the menarche. Diagnosis of chronic cervicitis and Trichomonas vaginitis was made. At this time, at the age of 26 years, she had a curettage and amputation of the cervix.

The gross pathological report described "a distinct erosion of the external portion of the cervix . . . sections through the cervix showed the stroma to be normal." It was also stated, "there was no gross evidence of malignant change," but this had never been considered and no biopsy performed. The pathologist's diagnosis was that of chronic cervicitis.

Upon admission she related that the bag of water had broken spontaneously at home an hour previously and that no contractions were yet perceptible. Abdominal examination revealed the height of the fundus to be 22 cm., the fetus occupying a left sacroanterior posi-

tion, with the fetal heart sound heard in the upper left quadrant. The cervix upon vaginal examination was small, very firm and fibrotic, evidencing no dilatation. During the next seven days the patient leaked amniotic fluid, demonstrable by the nitrazine test, intermittently and daily. Section was considered but conservative management decided upon. Finally, over eight and one-half days following admission she began to have regular contractions, the fetal heart sounds being present at the onset of labor. Following a first stage of 22 hours the patient delivered an assisted frank breech 1,559-gram stillborn infant. There was no laceration of the cervix or lower birth canal.

Summary

1. The incidence of successful pregnancy in the seven patients presented in this preliminary study was decreased from 91 per cent to 21.5 per cent by the operation of amputation of the cervix uteri.

2. The cesarean section rate was increased from 0 to 57 per cent following amputation of the cervix uteri, the only surviving babies in this series being delivered by this procedure.

3. Vaginal delivery following this operation was characterized by either a prolonged first stage or an increased latent period between rupture of the membranes and the inauguration of labor.

4. Two cases of parturition following amputation of the cervix are discussed in detail.

5. Among the cases reviewed in this study there has been found no difficulty in parturition following the Sturmdorf operation.

6. Amputation of the cervix uteri in any woman who may subsequently become pregnant is to be condemned strongly.

7. The Sturmdorf operation may be considered a safe alternative to amputation of the cervix in young women.

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ELECTIVE INDUCTION OF LABOR AT TERM*

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ELECTIVE induction of labor at term is a procedure that has been gaining in popularity and increasing in frequency during the past fifteen years. Evidence of this trend is to be found in the numerous articles on the subject in our current medical literature. Spontaneous labor is not devoid of risks to both mother and child. There must, therefore, be a certain calculable risk in labor that is started by artificial means. It is the purpose of this study to determine whether this risk is greater or less in those cases that were induced than in cases in which labor was not induced. To assess this risk 1,000 consecutive deliveries at St. Joseph Hospital have been analyzed from the maternal and fetal standpoints and the results are presented.

Since this procedure is purely an arrangement of convenience between the patient and the obstetrician, there are no absolute indications. It is my personal belief that a woman who has endured a pregnancy to term should be offered the option of being relieved at an appointed time, and for that reason I offer my patients the choice of induction or of continuing pregnancy until labor ensues. There are a number of contraindications: malpresentation, disproportion, obstruction of birth canal, presenting part not fixed in pelvic inlet, placenta previa (except marginal), or long rigid cervix.

There are three methods of induction, each of which has its advocates:

1. Medical induction with some form of pituitary substance, usually Pitocin. This method is not sure and frequently results in half-hearted attempts at induction which do not carry labor to a conclusion, to the disgust of the patient and the doctor, and too frequently results in the conclusion that, after a "trial of labor" which failed, cesarean is indicated.

2. Rupture of the membranes without any medication. This method is more certain of success than the first, but there is almost always an appreciable latent period before labor pains ensue. In some instances this latent period is prolonged to the distress of the patient and the discomfiture of the doctor.

3. Combined rupture of the membranes and the immediate administration of Pitocin. This method eliminates the latent period and the progress of labor can be quite adequately controlled by the amount and frequency of administration of Pitocin. This is the method used in the cases here reported. My procedure is very simple. Each patient who elects to have "labor by appointment" is instructed to enter the hospital at 8 A.M. without breakfast. She is given the routine preparation. Before examination she is placed on a bedpan and has a vaginal instillation of 15 c.c. of 5 per cent aqueous solution of merurochrome. Vaginal examination is then done with a sterile glove without further draping. The condition of the cervix, the presentation and the position and

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the station of the presenting part are determined. If these are all favorable, the membranes are punctured with a long curved intrauterine dressing forceps. If the cervix admits one finger readily, the forceps is passed along the finger and the membranes are punctured. If the cervix does not admit a finger, a large-size Graves' speculum is inserted and the cervix is exposed and the forceps is introduced by direct sight into the uterine cavity and the membranes are punctured. I do not attempt to produce a large rent in the membranes, but as soon as amniotic fluid appears the forceps is removed, and Pitocin, 2 minims, administered hypodermically. This is repeated every 20 minutes until labor is well established. This is a larger dose than is recommended in most articles on this subject, but in many years of use I have never seen a tetanic contraction of the uterus or too violent labor ensue following this routine. It is not always possible to rupture the membranes at the first attempt, in which case the Pitocin is given at the regular intervals, and at the next examination to determine progress of labor, rupture of the membranes is usually accomplished without any difficulty. Rarely the induction may be continued by the medical method without puncture of the membranes. All examinations throughout labor are performed vaginally, always preceded by the instillation of 5 per cent mercurochrome. Attempts at hurrying labor are avoided, and as soon as labor is definitely established with pains occurring every three to four minutes and progress in effacement and dilatation of the cervix taking place, the injections of Pitocin are discontinued.

TABLE I. 1,000 CONSECUTIVE DELIVERIES AT ST. JOSEPH HOSPITAL

	INDUCED	NOT INDUCED
Gravida i	103	272
ii	103	232
iii	48	95
iv	23	56
v	12	21
vi +	12	23
Total	301	699

The striking correspondence of the relative proportions in each category as to gravidity was purely a matter of chance. No attempt was made in selecting these cases to have a similar percentage of the groups.

TABLE II. LENGTH OF LABOR

HOURS OF LABOR	1-3	3-6	6-9	9-12	12-15	15-24
301 Induced.—						
Gravida i	5	15	20	29	13	17
ii	22	40	22	12	4	3
iii	13	10	12	10	0	3
iv	6	10	3	4	0	4
v	3	5	3	1	0	0
vi +	4	4	3	1	0	0
Total	53	84	63	57	17	27

HOURS OF LABOR	1-3	3-6	6-9	9-12	12-15	15-18	18-
699 Not Induced.—							
Gravida i	4	20	61	68	57	24	38
ii	7	92	90	25	9	7	2
iii	9	39	31	13	2	1	0
iv	7	25	15	7	1	1	0
v	1	12	4	3	1	0	0
vi +	6	6	7	1	2	1	0
Total	34	194	208	117	72	34	40

In Table II a comparison is made of the length of labor in the cases in which labor was induced and in those in which it was not induced. Also they are subdivided according to gravidity. When labor actually begins is a debatable question, especially in the group of patients in which labor was not induced. In every instance the patient was asked, "When did you first notice labor pains?" and the time was recorded. Quite probably in the extremely short labors the pains had not been severe enough for some patients to call them labor, and in all likelihood in some of the long labors the patients were not in labor at all when they thought they were. In the patients listed as having induced labor, none of them were actually having regular contractions, although the number of the short labors indicated at least the impending onset of labor.

TABLE III. 301 INDUCED LABORS

HOURS OF LABOR		1-3	3-6	6-9	9-12	12-15	15-24
Gravida	i	5	15	20	29	13	17
	ii	22	40	22	12	4	3
	iii	13	10	12	10	0	3
	iv	6	10	3	4	0	3
	v	3	5	3	1	0	0
	vi	4	4	3	1	0	0

NUMBER OF INJECTIONS PITOCIN* 2 MINIMS

HOURS OF LABOR		1-3	3-6	6-9	9-12	OVER 12	FAILED
Gravida	i	21	28	16	19	15	4
	ii	46	25	15	6	11	0
	iii	25	13	2	4	4	0
	iv	15	5	1	1	1	0
	v	5	2	4	1	0	0
	vi	5	4	3	0	0	0

*In 12 selected cases Pitocin, 0.5 c.c. in 500 c.c. saline, was used intravenously to induce labor. In 4 cases total dosage was 4 minims, in 6 cases total 6 minims, in 2 cases 10 minims. Length of labor ranged from 2 hours to 15 hours, average time being 5 hours.

This table shows the length of labor in the 301 induced labors and the number of injections of 2 minims of Pitocin required to establish labor and carry it through to delivery. Recently the use of solutions of Pitocin in dextrose and saline by the intravenous route has been tried in a limited number of cases. Pitocin, 0.5 c.c., is placed in the flask of 500 c.c. of dextrose in saline and given at the rate of 30 to 40 drops per minute. This has proved to be effective in the 12 cases included in this report. I have restricted this method of induction to the very obese patients in whom we have found that doses of 2 minims subcutaneously are completely lost in the fatty tissue. The intravenous method is possibly more efficient and perhaps more easily controlled than the hypodermic method, but it has the disadvantage of requiring the patient to lie quietly with the arm on the arm board for several hours, and if the patients becomes restless or unruly when sedation is administered it constitutes a nursing problem. We have no intention of using this method to replace the subcutaneous administration method, except when indicated.

Table IV shows the maternal complications in each group. The low incidence of toxemia is worthy of special attention, for in this series of cases no attempt was made to control weight gain, and no attempt was made to reduce obese patients. Patients were all advised to eat a balanced diet, which was supplemented with mixed vitamins and calcium and iron. Six toxic patients were judged to have a degree of toxemia severe enough to warrant induction; the other six cases were mild and the patients went into labor either early or at term. The one eclamptic patient was not seen in pregnancy until near term,

when she had convulsions at home and was brought to the hospital. She was treated in the usual manner, and when convulsions had been brought under control, labor was induced. Cesarean for the entire series is 2.6 per cent; in the induced group there were four cases, three in which induction either failed or the delivery was delayed to the point that section seemed the more conservative course. In the fourth case, a breech presentation, the cord prolapsed when the cervix was about 2 cm. dilated. Section was done, and the baby lived. There was one prolapsed cord in the group not induced, a vertex presentation, and the cord was not pulsating, and section was not done.

TABLE IV. MATERNAL COMPLICATIONS

	INDUCED	NOT INDUCED
Pregnancy toxemia	6	6
Eclampsia	1	0
Hemorrhage	2	10
Febrile puerperium	3	9
Laceration into rectum	0	2
Cesarean section	4*	22†
Breech presentation	13	21
Placenta previa	1	8
Abruptio placentae	0	1
Occiput position, Kjelland forceps	114	219
Maternal death	1	0

*Indications for cesarean, induced:
Induction failed 3
Prolapse cord 1

†Indications for cesarean, not induced:
Repeat section 6
Placenta previa 8
Cephalopelvic disproportion 6
Abruptio placentae 1
Hydrocephalus 1

There was only one maternal death in the entire series, and that occurred in the induced group. This patient was a 39-year-old gravida xii, at term. Labor was induced by Pitocin alone without rupture of the membranes. She had a total of 6 injections, 3 in the morning, and, as her pains subsided, she had 3 subsequent injections early in the afternoon. About 4:20 P.M. she suddenly became excited and apprehensive and promptly became very cyanotic. She was moved to the delivery room, and the membranes ruptured as she was being moved from the bed to the stretcher. Her respirations were rapid, and she was difficult to restrain on the delivery table. Oxygen was administered, and her color improved, and she became quiet. A very little anesthetic was administered, and I was able to deliver a living baby by assisted breech. Bleeding was about 500 c.c. The placenta was removed promptly, manually, and the uterine cavity was packed. Intravenous fluids were started, and 500 c.c. of blood were administered. Oxygen was given constantly. Her condition did not improve, and she died about two hours after the onset of symptoms. My two associates were called and arrived about the time delivery was completed. We all thought there was a possibility of a ruptured uterus, although I had palpated the uterine cavity prior to packing and did not feel any laceration. Permission for partial autopsy was obtained, abdomen only. There was no blood in the peritoneal cavity, and the uterus was not ruptured. There was a large intramural fibroid in the posterior uterine wall. It is impossible to be certain of the cause of death, but I strongly suspect that death was due to pulmonary embolism of amniotic fluid. The sequence of events, excitation, jactitation, and cyanosis, the improvement of her condition with oxygen, the development of shock, and death follow the pattern as described in this condition. If this diagnosis is acceptable, then it is probable that the embolism would have occurred had labor been spontaneous, and would probably not have occurred had I induced labor by puncture of the membranes.

In the induced group there was no normal baby who died in the neonatal period. In the not induced group there were 5 neonatal deaths, 2 of them as the result of erythroblastosis, and 3 unexplained either symptomatically or at autopsy.

TABLE V. FATAL COMPLICATIONS, PREMATURE INFANTS EXCLUDED

	INDUCED	NOT INDUCED
Stillbirth (macerated)	3	8
Neonatal death	2	5
(Anencephalic 1)		(Erythroblastosis 2)
(Achondroplasia 1)		

Summary

A study of 1,000 consecutive deliveries has been presented with an analysis of the results in 301 unselected cases in which labor was induced as compared with 699 not induced. In this series induction has been shown to be a safe procedure, with a slight tendency toward shortened labor.

Conclusion

Elective induction at term may safely be offered to those pregnant women who for reasons of convenience desire their delivery to be arranged for a certain day. I think we can assure the mother that the procedure will not put her life or health, nor that of her baby, in any greater jeopardy than would exist in a labor that begins spontaneously, and we can with reasonable confidence promise a somewhat shorter labor by the induction method.

The method of choice is the subcutaneous administration of Pitocin and the puncture of the membranes. Intravenous administration of Pitocin should be further studied and probably reserved for special cases.

My appreciation is due the Record Librarians at St. Joseph Hospital for making these records available for study.

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221 WEST CENTRAL AVENUE.

URINARY HISTIDINE AS AFFECTED BY MASSIVE DOSES OF PROGESTERONE IN PATIENTS WITH CARCINOMA OF THE CERVIX

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IT HAS long been recognized that there is an appreciable increase in the histidine excreted in the urine during the course of a normal pregnancy.[2, 7, 9] The daily urinary excretion of histidine has repeatedly been observed to rise from the normal nonpregnant range of 25 to 250 mg. per day to a higher range of 300 to 1,000 mg. per day during pregnancy.[10, 18] These variations were greater than could be explained on the basis of dietary intake.[18] This increase in urinary histidine has been advanced as the basis of several tests for pregnancy,[7, 13, 16] but has not gained wide acceptance.

Several explanations have been offered for this increased urinary excretion of histidine during pregnancy. Kapeller-Adler[8] has described a decrease in the activity of an enzyme, histidase, in the liver of pregnant subjects. According to this explanation, the decrease in the activity of histidase results in a decreased destruction of histidine in the liver with a consequent increase in the urinary excretion. Page[10] has reported an apparent lowering of the renal threshold of histidine during pregnancy which would result in a greater urinary excretion of histidine. He postulates that this is due to a decrease in the tubular resorption of histidine brought about by the large amounts of estrogen and/or progesterone secreted during pregnancy.[11] More recently it has been reported that the 24-hour urinary excretion of histidine and several other amino acids is increased in patients with arthritis,[6] allergy,[14] and mental diseases[12] treated with ACTH or cortisone. Venning[17] has reported an elevation in corticoids in the urine of pregnancy. This suggests the possibility that the increased excretion of histidine in pregnancy may be mediated by way of adrenal cortexlike hormones.

Members of our group[5] have been studying the effect of large doses of progesterone on carcinoma of the human cervix uteri. This afforded an opportunity to study the effect of exogenous progesterone on histidine excretion when administered in amounts approximating those produced endogenously during the course of a normal pregnancy. This study was thought to be of interest because of (1) the relationship of progesterone to pregnancy, (2) the slight corticoid activity of progesterone, and (3) the possible relationships of pregnancy and corticoids to the changes observed in the malignant lesions followed during this study.

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Procedure

Nine patients in good nutritional condition with carcinoma of the cervix, Grades I, II, and III, were admitted to the hospital and provided regular hospital diets ad libitum. After a control period of several days the patients were given daily injections of 250 mg. of progesterone* in oil intramuscularly for periods of 28 to 147 days. During the control period and several times during the course of the injections, determinations were made of apparent free histidine in 24-hour urine specimens.

Urine was collected for 24-hour periods and immediately refrigerated. The volume was measured and an aliquot preserved under toluene. The urine was then subjected to mild hydrolysis by acidifying to pH 4.0 with acetic acid and autoclaving for ten minutes at 15 pounds pressure according to the method of Harvey & Horwitt.[2] These specimens were then assayed for apparent free histidine by the microbiological method of Henderson and Snell[3] with the use of *Leuconostoc mesenteroides* as a test organism. After 72 hours incubation at 37° C. the amount of lactic acid was determined by titration with 0.1 N. sodium hydroxide. The end point of titration was determined with a micro-titrimeter[4] attached to a Beckman model G pH meter. All determinations were made in duplicate at three different dilutions of urine.

Results and Comment

The apparent free histidine content of 68 24-hour specimens was determined in nine patients before and after the administration of progesterone. Histidine determinations were also done on 24-hour urine specimens from three cases of normal pregnancy for purposes of comparison with the use of the same techniques (Table I).

Daily pregnandiol excretion was determined on six of these and six other patients receiving 250 mg. of progesterone daily as part of a study reported elsewhere.[5] The average of 192 determinations on twelve patients was 30 mg. per 24 hours. This is similar to the pregnandiol excretion found in the third to sixth month of pregnancy[17] when histidine excretion has been found to be high.

Since pregnandiol is the metabolic excretory product of progesterone, we believe that the 250 mg. dose of progesterone may approximate the amount produced endogenously during the third to sixth month of normal pregnancy. The average amount of pregnandiol excreted in the urine in this series of cancer patients was 10 per cent of the administered progesterone. This is approximately the same percentage of urinary pregnandiol found after the administration of progesterone to normal subjects.[15] Thus, the metabolism of progesterone in this group of cancer patients does not differ markedly from its metabolism in normal subjects as measured by pregnandiol excretion.

The 24-hour excretion of histidine in this group of cancer[18] patients falls within the range established for normal subjects. There was no increase in histidine excretion during progesterone administration.

The failure of large quantities of progesterone to cause an increase in urinary histidine suggests that (1) progesterone is not the element present in pregnancy which causes an increase in histidine excretion in patients who become pregnant, (2) the regressive changes observed in the malignant lesions during the courses of this study[5] do not occur as the result of simulation of the entire metabolic pattern of pregnancy by the administration of progesterone.

*Provided through the courtesy of Dr. E. E. Henderson of the Schering Corporation.

TABLE I. APPARENT FREE URINARY HISTIDINE IN PROGESTERONE-TREATED AND PREGNANT WOMEN (MILLIGRAMS PER 24 HOURS)

CASE	AGE (YEARS)	PRETREATMENT HISTIDINE (MG./24 HR.)	POSTTREATMENT HISTIDINE	
			NO. OF DAYS TREATED	HISTIDINE (MG./24 HR.)
E. G.	65	46, 31	28	67
G. H.	57	35, 40, 36	8	25
			12	44
			87	27
			88	24
C. M.	60	34, 45, 47	2	43
			5	48
			68	48
E. P.	31	146	1	127
			2	130
			3	165
			4	98
			5	131
			6	59
			7	90
M. P.	61	132, 100, 77	8	69
			15	26
			22	75
			29	60
			36	50
			43	75
			50	24
			57	70
J. S.	71	129, 155, 83	63	70
			65	65
			66	63
Z. S.	62	58, 49	8	116
			15	116
			22	84
			29	55
			36	17
			43	15
H. S.	23	282, 340, 268	82	152
			83	95
			84	129
			85	129
			86	86
			87	147
J. Y.	53	112, 50, 62	5	40
			9	33
			13	75
			17	69
			138	97
			146	67
			147	68
G. Y.*	26	1000		
L. H.*	30	450		
M. L.*	31	330		

*Urine from normal pregnancy cases.

Summary

1. The metabolism of histidine in pregnancy is briefly reviewed.

2. The apparent free histidine content of 24-hour urine specimens was determined microbiologically in 68 samples of urine from 9 patients with carcinoma of the cervix who were treated with large doses of progesterone.

3. The values obtained for 24-hour excretion of histidine fell within the range established for normal subjects and did not rise following the administration of massive amounts of progesterone.

4. Progesterone is apparently not the factor which brings about an increase in the histidine excretion in pregnancy.

5. The regressive changes observed during administration of progesterone do not result from the complete reproduction of the metabolic status of the pregnant individual.

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PUDENDAL BLOCK WITH HYALURONIDASE*

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THIS is the second report of a study of pudendal block with 1 per cent procaine and hyaluronidase. The cases are 250 completely unselected service cases, 200 blocks with hyaluronidase and 50 blocks without.

The enzymatic action of hyaluronidase hydrolyzes hyaluronic acid, a viscous polysaccharide found in the interstices of the tissue, where it normally obstructs diffusion of invasive substances. The basic research defining the properties of hyaluronidase apparently arose from the observations made as early as 1928 by Duran-Reynals.[1] It is reasonable to imagine that the enzyme would be applied, if possible, to increase the penetration of desired substances into the tissues. That this has been feasible seems apparent from the number of papers relating to the use of hyaluronidase in hypodermoclysis.[2-3] Hyaluronidase has been discussed favorably as an adjunct to local anesthesia in dentistry and numerous surgical conditions. The study[4] of the action of epinephrine on the spreading factor is of interest. It seems that if a vasoconstrictor would decrease the absorption effect, it might also decrease the spreading effect. This apparently is not so. The spreading effect, on the contrary, appears to be enhanced by epinephrine. Presumably this is because the rapid absorption caused by the hyaluronidase prevents the maximum spreading which occurs when absorption is delayed by a vasoconstrictor.

Pregnant women should be psychologically prepared for a certain amount of discomfort in labor and be told that a moderate amount of pain is normal. Most women fear labor pains and that fear is responsible for much of their suffering. These women should learn that everything will be done for them that is compatible with safety for them and their infants. They should understand the doctor's basis on which he hesitates to relieve the pain of labor completely. Pudendal block anesthesia for delivery and repair is a near-perfect anesthetic for the patient, the fetus, and the doctor. The outstanding feature of the method is that marked perineal gaping occurs within three minutes after the injection takes place. This facilitates a low-forceps delivery, makes delivery of a breech easier, and minimizes perineal lacerations. The perineal reflex and the resultant urge to bear down are lost. The patient has to be instructed to bear down to help deliver the child. The pain of perineal stretching will be avoided. This pain is by far more severe than the other pain associated with labor, such as backache and abdominal pain. If this perineal pain is controlled, the patient does not suffer.

*Wyeth, Incorporated, generously supplied the hyaluronidase in the form of Wydase for this study.

The popularity of regional anesthesia has been limited, because of the inability of surgeons and anesthetists to deposit anesthetic solutions accurately and consistently along nerve trunks. Even skilled anesthetists cannot obtain adequate blocks in all instances. This method of increasing the diffusion of local anesthetic agents, therefore, might be of value in producing a higher percentage of successful blocks. In certain instances, increased diffusion might also be helpful in infiltration anesthesia. In a recent publication, Eckenhoff and Kirby[5] concluded that the addition of hyaluronidase did not increase the incidence of successful blocks. It is interesting that in their large series of nerve blocks (208) pudendal block was not included. It has been theorized that fascial planes do not play an important part in anesthetizing the perineum. However, these fascial planes do apparently in the region of the cervix. Since this study began, hyaluronidase was added to the anesthetic mixture also for paracervical blocks for dilatation and curettage of the uterus. Paracervical blocks with the addition of hyaluronidase do not appear more effective than those blocks that were done without it. This does not hold, however, for pudendal block.

Technique

The anesthetic mixture is made up by addition of the contents of one vial of lyophilized hyaluronidase (150 T R units) and 0.5 c.c. of epinephrine (1:1,000) to 30 c.c. of 1 per cent procaine. The vial contains 150 turbidity reducing units of hyaluronidase, such a unit being defined as the amount of hyaluronidase that reduces the turbidity caused by 0.2 mg. of hyaluronic acid in horse serum to that caused by 0.1 mg. Intradermal wheals of the mixture are made halfway between the anus and ischial tuberosities on the perineum. A 10 c.c. Luer Lok syringe with a spinal No. 20 needle is used. Two fingers are placed in the vagina for orientation during injection. Starting through the wheal, the needle is passed to the tuberosity and 5 c.c. of the anesthetic solution are placed posteriorly and medially to the tuberosity to anesthetize the perineal branch of the posterior cutaneous femoris nerve. Then the needle is passed horizontally to the ischial spine and 5 c.c. of the solution are deposited here to anesthetize the pudendal nerve as it enters Alcock's canal. The syringe is then taken off the needle and refilled. Five c.c. of mixture are then infiltrated in the superior portion of the labia minora to anesthetize the perineal branches of the ilioinguinal nerve. The same procedure is carried out on the other side of the perineum. Complete perineal anesthesia is practically instantaneous. This is one definite advantage of the hyaluronidase mixture. One can secure an effective block more quickly than with the ordinary-type anesthetic mixture.

Results

	HYALURONIDASE ADDED (200 CASES)	CONTROL (50 CASES)
Parity of Patients.—		
Primagravidas	82 (40%)	22 (44%)
Multigravidas	118 (60%)	28 (56%)
Type of Delivery.—		
Spontaneous	137 (70%)	30 (60%)
Low forceps	63 (30%)	20 (40%)
Episiotomies	110 (55%)	36 (72%)
Duration of Anesthesia.—		
Longer than 45 minutes	156 (80%)	13 (26%)
Less than 45 minutes	44 (20%)	37 (74%)

Using Farr's description of an ideal and successful anesthetic, as one in which the operative procedure was completed with no pain or discomfort to the patient, a satisfactory anesthesia is one in which the indicated procedure was completed with only a slight amount of discomfort, and a failure as a case where local anesthesia had to be abandoned or supplemented with inhalation anesthesia, we had the following results:

FINAL END RESULT	HYALURONIDASE ADDED (200 CASES)	CONTROL (50 CASES)
Ideal	160 (80%)	14 (28%)
Satisfactory	30 (15%)	26 (52%)
Failure	10 (5%)	10 (20%)

Although a small number of cases, this compares favorably with statistics given by Buxbaum[6] at the Chicago Maternity Center, where local anesthesia is strongly advocated.

FINAL END RESULT, BUXBAUM	
Ideal	880 (40%)
Satisfactory	1,210 (55%)
Failure	110 (5%)

Summary

The ideal agent to employ routinely in order to obtain analgesia and/or anesthesia in obstetrics has yet to be found.[7] Requirements for the perfect analgesic drug or method are as follows:

1. It must be quick in action, constant, and not complicated in administration.
2. It must not interfere with the progress of labor.
3. It must be nontoxic, to both the mother and fetus, and there should be a wide margin between the toxic and therapeutic doses.
4. It must produce an amnesic as well as analgesic effect.
5. It should produce complete relaxation without destroying the patient's ability to cooperate.
6. It should not lead to postpartum bleeding, excitement, or other complications.

A variation of a method of regional anesthesia is presented. The effectiveness of this procedure over regular pudendal block will become obvious even in the hands of a novice. Above all, it facilitates relief of pain of perineal stretching, which can only be otherwise obtained with the more formidable types of anesthesia. We have seen no untoward reaction or contraindications toward its use. We speculated about the 0.5 c.c. (1:1,000) of epinephrine added to our mixture having a vasopressor effect on our hypertensive patients. We have seen no appreciable rise in blood pressure. There were no local or systemic reactions to the use of the drug. No effort was made to skin test the patient prior to delivery. All episiorrhapies healed by primary intention and there were no local infections or ecchymoses of the perineum. The tech-

nique of pudendal block is greatly simplified. The operator does not have to inject the nerve per se, but infiltration in the vicinity of the nerve will accomplish an effective block. It is impressive to see interns, new to the obstetrical service, secure successful nerve blocks during their first attempts at pudendal block. After use of some basic analgesia during the first stage in combination with this regional block for delivery, the child breathes spontaneously and immediately, and the mother has no nausea or vomiting following delivery.

Conclusions

1. Hyaluronidase is a useful adjunct to the anesthetic mixture for pudendal block since a much higher percentage of ideal blocks was secured with hyaluronidase (80 per cent) than without this drug added to solution (28 per cent).

2. There is a very rapid onset of anesthesia.

3. A much smaller amount of anesthetic solution is necessary for adequate blocks.

4. There were no local or systemic reactions to the hyaluronidase.

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INTRAVENOUS ALCOHOL USED FOR PREINDUCTION ANALGESIA IN OBSTETRICS*†

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INTRAVENOUS alcohol has been used in surgery as a postoperative analgesic for many years. Although there have been periods of great enthusiasm among a few, intravenous alcohol as a postoperative analgesic has never been generally accepted. Recently, intravenous alcohol has gained new supporters in general surgery. Belinkoff and Hall have reported its use, with varying results, in a small number of obstetrical cases. They state that "the administration of intravenous alcohol in our hands has not proved to be the ideal method for the relief of pain of childbirth."

Early in our work we, too, used intravenous alcohol during active labor for the purpose of producing analgesia and amnesia. Numerous disadvantages were found with this method of treatment. During the administration of intravenous alcohol, constant supervision of the patient was necessary in order that the intake would not be in excess of the patient's tolerance; any excess dosage would cause vomiting and labor would stop. This occurred in spite of watchful efforts. However, amnesia and analgesia were not frequently encountered even though large quantities of fluid were administered. Patients also were disappointed at not being relieved of their pains as compared to their previous labors.

Although many disadvantages were encountered, we were impressed with the good perineal relaxation, the smoother induction, and the early response of the babies. We, therefore, believed that intravenous alcohol had many commendable features and that it deserved further investigation. For this reason, we began using it as a preinduction analgesic; this method serves as the basis of our report.

Procedure

The cases here presented are unselected and may represent either private or ward patients. No attempt was made to eliminate complications, although a few did appear. A 5 per cent solution of alcohol in water and 5 per cent glucose was given through an 18-gauge needle which had been inserted into one of the antecubital veins. This process was begun when the cervix was fully dilated or nearly so, and the presenting part was near the perineum. The alcohol was run into the vein quickly for the first 200 to 500 c.c., depending upon the nearness of the delivery and the effects desired. At this time the drop ether-oxygen anesthesia was begun. The flow was then regulated according to the patient's

*Read before the Pittsburgh Academy of Medicine, May 8, 1951.

†The 5 per cent alcohol in water and 5 per cent glucose were graciously furnished by the Abbott Laboratories, North Chicago, Ill.

reactions; larger quantities were rapidly injected without danger, provided the flow was stopped when nausea appeared. The average patient received 436 c.c. of intravenous alcohol, 35 minutes prior to the beginning of drop ether-oxygen anesthesia. The extremes were ten minutes to two hours and 100 c.c. to 1,000 c.c. of alcohol.

Premedication, such as Nembutal, scopolamine and Demerol, was given to the patient as was believed necessary, disregarding the possibility that alcohol might be given.

Only cord blood specimens were taken for alcohol determinations upon the baby (Bogen's test).

Results

We have now limited the use of intravenous alcohol to preinduction analgesia and are impressed with its several advantages.

All babies upon delivery are of a nice pink color, 75 per cent of them needed no aid, 15 per cent were given some oxygen inhalations, and 10 per cent were resuscitated. No distress was seen at any time; however, occasional sluggishness was noted. We believe that this is a definite improvement over past experiences where similar methods of premedication were used.

The absence of vomiting, we believe, is one of the outstanding advantages of intravenous alcohol. In only three cases was minimal vomiting encountered.

After approximately 100 to 500 c.c. of intravenous alcohol were given, the patient was more smoothly and easily anesthetized. The desired plane of anesthesia was maintained with little difficulty. It was first brought to our attention by the Anesthesia Department that less ether was used by this method. An average of 0.097 oz. per minute of ether was used in our series, and 0.170 oz. per minute of ether in a control series. The period of recovery from anesthesia was very smooth and the patient continued a restful, quiet sleep from 15 minutes to 2 hours.

TABLE I. RESULTS

	NO.	VOMITED	GOOD PERINEAL RELAXATION	RESUSCITATION NECESSARY	SMOOTH INDUCTION	PLEASANT UNEVENTFUL RECOVERY
Primiparas	15	0	40%	20%	80%	100%
Multiparas	30	10%	90%	0	90%	100%
Total	45	6.5%	74%	6%	86%	100%

Comment

We have tempered our observation with conservatism because of our enthusiasm for intravenous alcohol as a preanesthetic agent. The almost complete absence of vomiting and the quiet, restful sleep following ether-oxygen anesthesia were the outstanding features of this report.

We believe that the babies responded more quickly upon delivery and that the perineum was markedly relaxed, but personal evaluation is a varying factor and additional studies are required.

Alcohol determinations were done on the cord blood, this being negative in 50 per cent and a slight trace in the remaining cases. As stated above, less ether was used than in the control group, but the difference does not seem to be statistically significant. Additional studies may confirm the belief that less ether was used.

In a few cases where labor was being induced by intravenous Pitocin, intravenous alcohol was simultaneously given for the relief of pain. The combination may prove of value when induction of labor is contemplated. The effects were gratifying but constant supervision was necessary.

One patient of this series was progressing satisfactorily in labor when the uterus began to contract rapidly; this progressed almost to a state of tetany of the uterus. Intravenous alcohol was immediately given as rapidly as possible through an 18-gauge needle and within two to three minutes the uterus relaxed and then continued to contract normally. She delivered spontaneously a normal child, one-half hour later without further difficulty. The ability of alcohol to slow or stop uterine contractions may occasionally be of value in such instances.

We encountered two cases of retained placenta and four cases of excessive bleeding (not hemorrhage) in this series. They were treated effectively without further difficulty.

Conclusion

We feel that in the light of this preliminary study the use of intravenous alcohol as a preinduction analgesia has the following advantages:

1. The almost complete absence of vomiting.
2. Decrease in the number of babies requiring resuscitation.
3. Smoother induction.
4. Restful sleep following delivery.
5. Increased perineal relaxation.
6. Possible decrease in the amount of ether required.

Addendum

Since this paper was written we have continued our work with intravenous alcohol and the results have been similar to those just reported. Chapman and Williams in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY of March, 1951, have recommended the use of intravenous alcohol during labor, in contradistinction to the belief of Belinkoff and Hall. Despite this report we wish to re-emphasize that intravenous alcohol may only be used to advantage as a preinduction analgesic during labor.

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CLINICAL EXPERIENCE WITH METHYL ANDROSTENEDIOL*

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METHYL androstenediol is a steroid closely related chemically to methyl testosterone and apparently sharing some of testosterone's actions [17(α)-methyl-Δ⁴-androstene-3-one-17(β)-ol and 17(α)-methyl-Δ⁵-androstene-3(β),17(β)-diol]. It is desirable to determine whether this steroid can be substituted therapeutically for testosterone in situations in which testosterone has been employed but has produced an undesirable complication of virilism. Screening tests have indicated that methyl androstenediol promotes growth (as shown by weight gain) in mice.[7] Though classed as an androgen, this steroid has considerably less androgenic activity than testosterone on secondary sex organs of test animals.[8] According to Gordan and associates,[1] it shows a myotrophic action in test rats, and Homburger and associates[5] have recently shown that it has a renotrophic effect in rats. Preliminary clinical reports indicate that it shares to some extent the anabolic action of testosterone, and this has been achieved without significant virilism in the women treated.[1, 2, 6] Therefore, there appears to be encouragement for further clinical appraisal.

There are numerous situations in which a steroid of this type might be employed therapeutically, and we have tested it in a total of 53 female patients with various complaints, in an effort to sift out those conditions in which methyl androstenediol therapy seems sufficiently promising to warrant further and more intensive study. Not all the patients have had the therapy for sufficient time to warrant conclusions. The present report will, therefore, be confined to those patients in whom results appear reasonably definite.

Thus far, it is clear that none of the 53 female patients treated with this chemical has shown toxic or untoward effects. None have shown any sign of virilism, such as an increase of hirsutism or enlargement of the clitoris. With comparable doses of testosterone derivatives, in this period of time, a few among this group of patients would have been expected to show definite virilism stigmas. One patient given a total of 2,800 mg. during a period of 60 days did not show any signs of virilism.

Subjective responses have been favorable. There has been a general trend for the patients to state they have "felt better," and they have claimed to have increased ambition and enthusiasm. This is also the usual result of testosterone therapy in this type of woman. Treatment of several patients has been completed for 3 to 4 months and none has experienced a return of previous symptoms. Some of the patients have stated that their breasts seemed less firm during methyl androstenediol therapy.

The conditions in which methyl androstenediol has been employed therapeutically and the results and impressions obtained are as follows:

*The methyl androstenediol was supplied by Organon, Inc., under the trade name of Stenediol.

Tender, Nodular Breasts.—Six women who had tender, nodular breasts, with a diagnosis of chronic cystic mastitis, were successfully treated with methyl androstenediol in a dosage of 25 mg. three times a week for two months. The three patients who had recent cystic development showed no palpable or tender areas at the end of the month of therapy. The three others were improved and without tenderness in the breasts.

We also administered methyl androstenediol therapy to 3 woman who complained of hypersensitivity of the breast during the premenstrual phase of the cycle. They were made completely comfortable in this therapy with doses of 25 mg. daily from the eighteenth to twenty-eighth days of the cycles.

Hyperestrinism and the Vaginal Smear.—Methyl androstenediol has the same effect on the vaginal smear as has testosterone. After a therapeutic dose of testosterone, there is at first an estrogenic type of response, but after larger doses there is a reduction in the number of cornified cells.

Relative hyperestrinism was controlled promptly in 6 of 8 patients after doses of 150 to 200 mg. of methyl androstenediol. Two required longer treatment for appreciable results.

"Relative" hyperestrinism might be classified as resulting from adequate pituitary follicle stimulating hormone function, but occurring while there is a deficiency of luteinizing hormone secretion, or during some anovulatory ovarian cycles. During such cycles, the endometrium continues to be of estrogenic type until menstrual bleeding is well established. This results in sterility and occasionally in prolonged or excessive menstrual bleeding. Such conditions may also be classified as hypoprogestational, providing that there is a high estrogenic type of vaginal epithelium at the same time.

As yet, no case of "actual" hyperestrinism, due to some types of ovarian tumors, has been tested here with methyl androstenediol.

The hyperestrinism in these patients was shown objectively by a continuous finding of hyperestrin type of vaginal cells throughout the nonbleeding phases of the ovarian cycles.

Subjectively, the complaints included occasional periods of excessive or extended flow. Menstrual irregularities are not unusual, due to the prolonged action of estrogen. Overly sensitive breasts may or may not occur, but if hypersensitivity is present premenstrually, methyl androstenediol corrects it.

The effect of the chemical was shown by a return to the normal cyclic phases of vaginal epithelium, and by relief from the complaints, objectively and subjectively.

Menometrorrhagia.—Four women with this condition were treated, but the results were variable. One of these patients responded following treatment during one ovarian cycle with 25 mg. daily for 8 days; two patients received 25 mg. daily, beginning on the first day of menstrual flow, for two weeks, during two cycles; one patient who complained of severe bleeding for 3 of each four weeks received prolactin during the normal phase of menstrual flow, followed by 25 mg. of methyl androstenediol daily during the rest of the cycle. All were successfully controlled.

Physical Exhaustion.—Four "exhausted" women, aged from 26 to 37 years, were treated with methyl androstenediol employed in the place of testosterone. The usual dosage given these patients was 25 mg. daily. Improvement was noted within one month of therapy and all described an improvement in vigor and ambition. They reported a greater initiative in their household duties and that their muscular strength seemed to be greater. This effect seems in accordance with an anabolic and myotrophic effect of the steroid, as evidenced in most of the patients treated in this study group.

This therapy was also employed with 7 debilitated menopausal women, and all of these showed similar improvement.

After Masculinization Following Testosterone Therapy.—Three women who had been treated with testosterone to reduce cystic breast disturbances showed hirsuties and considerable hypertrophy of the clitoris. In the place of testosterone they were given methyl androstenediol in the following dosage: 25 mg. doses were administered intramuscularly once a week and 25 mg. daily in buccal tablets for 3 of each 4 weeks. There was a gradual but rapid reduction in the size of the clitoris, and the hirsuties did not progress, while at the same time the breasts remained reduced in size. The desired antiestrogenic effect, as shown by the vaginal smear, continued to be noted.

Fibromyoma of the Uterus.—Four patients with easily palpable fibromyomas were treated with methyl androstenediol in the following dosage: 25 mg. intramuscularly three times weekly. Continued antiestrogenic effects were noted physiologically in a reduced size of two fibroid tumors in this group, and the maintenance of basal-cell types of epithelium for one patient who had cervical carcinoma. To one patient who had a walnut-sized fibroid, a total of 850 mg. of methyl androstenediol was administered during three menstrual cycles, at the end of which time the fibroid was no longer palpable. In the three other patients, who had multiple and sizable tumors, after 7, 9, and 16 weeks there was a definite reduction in the size of the fibroid tumors, according to palpation. This result seemed impressive, and is even better than the results obtained following prolactin and equine gonadotropin as previously reported.[3, 4]

It is considered probable that methyl androstenediol can completely replace the use of testosterone for the purpose of controlling the unbalanced chemistry that permits fibromyomatous growths. It is also probable that long-continued prolactin therapy will no longer be necessary for this purpose. During recent years only 17 per cent of uterine fibroid patients have been subjected to surgery. It seems probable that the use of methyl androstenediol as part of the treatment may reduce that figure even lower.

Case Reports

Uterine Fibroid.—A mother, aged 40 years, had a palpable "hen's-egg-size" fibroid on the anterior wall of the fundus of the uterus, and the vaginal epithelium showed signs of hyperestrinism. During a period of five months, 2,825 mg. of methyl androstenediol were administered at the rate of 150 mg. per week, intramuscularly and buccally. During the first 2 weeks of treatment, she also received 200 mg. of testosterone. At the end of the five months' period of treatment, the fibroid mass was no longer palpable. The vaginal mucosa was interpreted as showing a low level of estrogen action, as almost all of the cells were of the basal type. The patient showed no signs of virilism. Her cycles had not been disturbed.

Cystic Breast Disease.—An unmarried woman of 21 years of age had a sizable mass in one breast, estimated to be 2.5 cm. in diameter. She was treated with one dose of 50 mg. of testosterone by injection, followed by 400 mg. of methyl androstenediol buccally per month during a period of three months. After the first menstrual cycle, the mass was noted to be one-half its former size, and at the end of three months this mammary gland was normal to palpation. Three months later, with no treatment, the breasts had remained normal.

Menometrorrhagia.—A nullipara, aged 35 years, had very profuse menstrual bleeding each month, lasting 10 days, followed by staining and spotting until midcycle, when three more days of heavy bleeding occurred. She had a small uterus without endometrial hyperplasia, and the vaginal mucosa showed a low level of estrogen action. Methyl androstenediol in a total dose of 125 mg. was administered during two weeks, intramuscularly, and the uterine bleeding stopped. At the end of this time, her breasts appeared smaller. With no further steroid therapy, her menstrual cycles were normal and regular for the succeeding three months.

Melancholia and Hyperestrinism.—A mother, aged 43 years, had become habituated to the daily consumption of 12 ounces or more of whiskey, and after ten months of this was markedly debilitated, and undernourished, and showed severe mental depression and melancholia. Testosterone therapy had been employed, but this quickly caused masculinization symptoms, and estradiol therapy appeared to aggravate the frequency and severity of her attacks of weeping. Methyl androstenediol therapy, 25 mg. intramuscularly twice a week for three weeks, was followed by marked improvement in her mental outlook. At the end of three weeks, normal menses occurred, without dysmenorrhea, and she claimed this was the first time in her life she had been without menstrual cramps.

Methyl androstenediol therapy was then given at weekly intervals during the next three ovarian cycles, and during this time she regained her weight and the strength that she had lost. Now she appears to be living a normal life. During this steroid therapy, she was also given the usual supportive and dietary treatment which, however, did not seem to be helpful until after the methyl androstenediol had been started. It was only after the first 75 mg. of methyl androstenediol were used that she showed the first indications of improvement. Alcoholism in this case had not yet become habitual, so far as could be told, and the patient's will was such that with improvement in her general physical condition, there was apparently no further craving for alcohol.

Conclusion

Methyl androstenediol therapy has been employed during the treatment of 53 female patients who had various disturbances for which testosterone therapy has been or may be applied. Methyl androstenediol appears to have accomplished what testosterone does, in most of the cases treated, and, yet, in the series of cases treated to date, no signs of virilism have appeared. Indeed, in 3 patients who showed virilism with testosterone, there was a reduction in these signs after methyl androstenediol therapy was completed.

The action of methyl androstenediol which appears to be most useful is the same as that expected from an anabolic and myotrophic action, such as an improvement of mental outlook, restored sensation of physical well-being, and greater muscular strength and endurance.

These case studies have shown sufficiently encouraging results to warrant further investigation of this steroid.

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626 Medico-Dental Building

ABSORPTION OF PENICILLIN THROUGH THE HUMAN VAGINA*

II. 500,000 Units of Penicillin at One Administration

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IN A previous study by us[1] 16 patients were tested for absorption of penicillin through the vaginal mucosa. All of these patients were ambulatory. A single 100,000 unit cocoa-base vaginal suppository was self-administered on a scheduled program. The blood levels varied, were inadequate therapeutically, and the rate of absorption was unpredictable. At about the same time Goldberger, Walter, and Lapid, using 500,000 units of penicillin in similar suppository form per vaginam, obtained therapeutic or adequately high levels of penicillin in the venous blood. Even so, these levels were maintained only a few hours. This report is a further investigation of the vaginal insertions as a possible route of administration for therapeutic blood levels by the method and dosage of Goldberger, Walter, and Lapid.

Material

A total of 20 patients were used for the observations for absorption of penicillin through the vagina. All of these patients were hospitalized on the obstetrical and gynecological services for conditions other than vaginal infections. Seven of these patients had undergone either natural or surgical menopause. Four patients had incomplete abortions. The remainder had menometrorrhagia or amenorrhea. The ages ranged from 22 to 55 years (Table I).

TABLE I. RELATION OF MENACMIC PHASE TO MAXIMUM BLOOD LEVELS

UNIT NO.	AGE (YEARS)	OVARIAN ACTIVITY	MAXIMUM BLOOD LEVEL
407553	45	5th day cycle	0.64
406032	46	7th day cycle	0.254
113692	30	12th day cycle	1.024
411660	44	15th day cycle	1.024
413969	26	16th day cycle	1.024
411403	45	26th day cycle	2.048
398830	28	Postmenopausal (surg.)	0.512
407876	31	Postmenopausal (surg.)	1.024
416623	31	Postmenopausal (surg.)	0.128
407867	34	Postmenopausal (surg.)	0.032
389062	52	Postmenopausal	0.256
373299	54	Postmenopausal	1.024
395484	55	Postmenopausal	0.128
412717	22	Incomplete abortion (postabortal)	0.512
415465	30	Incomplete abortion (postabortal)	1.024
275811	32	Incomplete abortion (postabortal)	1.024
355511	26	Missed abortion	0.512
115172	34	Amenorrhea	0.256
39069	47	Metrorrhagia	1.024
372152	27	Endometriosis	0.128

*Supported in part by The Chicago Lying-in Hospital Fiftieth Anniversary Fund for Research on Puerperal Infection.

Five cocoa-base penicillin suppositories, 100,000 units each, were placed in the vaginal vault by one of us (M. S.). Every patient was kept in bed for the duration of the tests. Five blood samples were taken on each of 4 patients at one-hour intervals to determine time of maximum absorption. The results closely approximate those found by Goldberger, Walter, and Lapid and Rach, Baker, and Bacon. The remaining 16 patients had 3 blood samples each, taken at 1½-hour intervals. The first sample was taken 1½ hours after insertion of the suppositories.

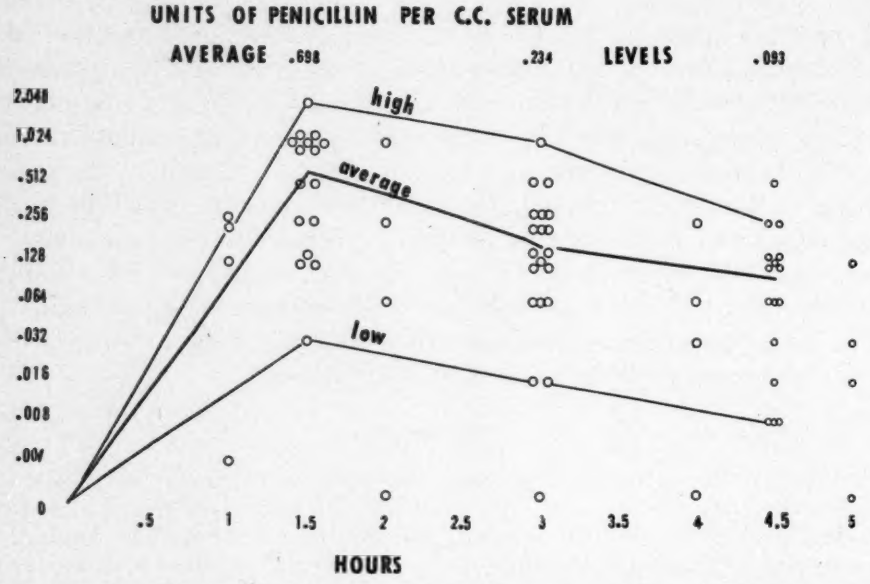

Fig. 1.—Serum levels attained with 500,000 units of penicillin single-dose vaginal suppositories.

The level of penicillin in the blood was determined by the test tube dilution method of Kolmer. All tests were run in duplicate. The Oxford strain *Staphylococcus aureus H.* was used as test organism. Tests with known dilutions were made at the same time to assure stability of the test bacteria.

Maximum level attained was 2.048 units of penicillin per cubic centimeter of serum at 1½ hours after insertion of suppositories. The average level was 0.698 unit per cubic centimeter of serum. This average level was determined in the 16 patients whose samples were drawn at 1½-hour intervals. The graph (Fig. 1) reveals the individual levels and variations.

With but few exceptions therapeutic blood levels were attained within 1½ hours and tended to be maintained during the next 3 hours for most penicillin-sensitive bacteria. Factors which did not appear to affect absorption of the drug were: age of the patient, day of menstrual cycle, menaemic and postmenopausal states (Table I).

No attempt was made to evaluate efficacy of treatment for local conditions in the vagina or infections elsewhere in the body as this was a pilot study to determine venous blood levels as an index of absorption from the vagina. In a previous study by us penicillin suppositories of 100,000 units did not yield distinct clinical benefit.

Conclusions

Therapeutic levels of penicillin in the blood stream were reached, and it would seem that such levels could be maintained if a sufficient number of

vaginal suppositories were used at regular time intervals. Maximum absorption was found at the first 1½-hour interval in patients kept in bed during the test period. It is estimated that it would require up to 20 suppositories of 100,000 units to maintain therapeutic levels for each 24-hour period. Such a number would be most inconvenient and unpleasant. The vaginal route for application of penicillin is inefficient and financially extravagant. Therapeutic blood levels have been maintained with approximately ⅒ the amount of drug when given intramuscularly. No untoward results were noted either in the vagina or elsewhere. No contraindications to vaginal suppositories were discovered under conditions of the experiment. The only indication evident would be for infection of the vagina caused by penicillin-sensitive bacteria. Syphilis, gonorrhea, and upper genital tract infections caused by penicillin-sensitive organisms should be treated by the parenteral method until data have been compiled which would demonstrate the wisdom of this deviation. The facts (1) that there are bacteria found frequently in the vagina which are penicillin resistant and (2) that some produce a penicillinase, would raise additional objections to this route of administration for systemic benefit.

We thank the Schenley Laboratories for their generous supply of penicillin suppositories.

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THE EFFECT OF TOXEMIA OF PREGNANCY ON THE NEWBORN

A Preliminary Report

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IT IS a well-observed fact that infants born to mothers suffering from toxemia of pregnancy are frequently difficult babies to get started in life. Toxemia is a frequent cause of prematurity, and even when a mother who is toxic does deliver at term, the baby is very often scrawny and shows signs of faulty nutrition in utero.

Our interest in this effect of toxemia was heightened when in March, 1947, an infant was delivered and died shortly thereafter with the clinical signs of uremia. Autopsy of this infant showed findings that would seem to indicate an intrauterine toxicity.

In the succeeding years we have had the opportunity to collect fifteen cases of true toxemia of pregnancy, and analysis of the cord bloods of these infants seems to indicate that in approximately 50 per cent of the cases there was a definite elevation of the uric acid content of the blood.

The original case as well as the findings in subsequent cases make up the subject matter of this paper.

CASE NO. 78597.—Mrs. D. A., a 28-year-old primigravida, was first seen on Jan. 8, 1947. Her last menstrual period was May 19, 1946; the expected date of confinement Feb. 26, 1947. Her weight was 176½ pounds, height 5 feet, and blood pressure 140/80. There was no albumin or sugar in the urine. Her blood was Rh positive, type II-A, and Hinton negative. She was seen again on Jan. 23, 1947, at which time there was 2-plus pitting edema of the hands and feet, and her weight was 181½ pounds. Her blood pressure was 130/80. On Feb. 13, 1947, her weight had jumped to 189 pounds, her blood pressure was elevated to 160/90, there was a 2 plus pitting edema of hands and feet, and the urine showed a 1 plus test for albumin.

She was placed on ammonium chloride, bed rest, and salt-free diet, and was followed at home. During the following week the edema subsided, the blood pressure dropped to 146/86, and she lost 10 pounds in weight. The urine showed a trace of albumin.

On March 4, 1947, the membranes ruptured spontaneously, and she was admitted to St. Elizabeth's Hospital with an unengaged breech, the cervix one finger dilated and fairly well effaced. Her blood pressure was 162/84, and the urine showed a 3 plus albumin.

A low transverse cervical cesarean section was performed and a 4 pound, 8 ounce male infant was extracted. The mother ran a rather stormy postoperative course for the first 6 days, with elevation of temperature and malaise.

The infant was seen by a staff pediatrician who noted that he was fairly well developed and markedly jaundiced, exhibiting marked carpopedal spasm on compression of the radial and dorsalis pedis vessels. There was marked twitching of the extremities. Physical examination was otherwise normal. A diagnosis of prematurity with probable infantile tetany was made.

The infant was given nothing by mouth until 3:00 P.M. March 6, 1947; then was placed on 2 per cent milk. Red blood count at that time was 6 million and the hemoglobin 22.4 grams.

On March 6, 1947, the baby began to exhibit twitchings, and bleeding from the mouth. The jaundice became very intense. Physical examination revealed suppression of breath sounds and fine crackles in both lower lung fields.

Calcium chloride, 15 grains, was given by mouth at 10:00 A.M., and 1½ ampule of caffeine, 0.25 Gm. intramuscularly at 11:00 A.M. The infant died at 3:25 A.M. On March 7, 1947, a clinical diagnosis of prematurity and cerebral hemorrhage was made.

Autopsy was performed on March 8, 1947, by Dr. John Larkin. The report will be confined to the structures showing pathological changes.

There was no fluid in either pleural cavity or pericardium. The lungs together weighed 46 grams. They were dark red, firm, and airless. All lobes sank in water. The cut surface was dark red and moist, exuding bloody fluid. After one lobe was forcibly inflated, it floated readily and became light pink in color. The trachea and bronchi were empty, of expected caliber, and lined by unaltered mucosa. There was no obstruction. The hilar lymph nodes were not unusual.

The kidneys together weighed 30 grams. The capsules stripped readily, revealing smooth dark red surfaces demonstrating fetal lobulations. On section the parenchyma was markedly hyperemic. There was indistinct corticomedullary differentiation. Each papilla of each kidney was orange-yellow in color, the color being due to streaks of yellow material radiating fanwise up into the pyramids. The pelves were undiluted. They contained a small amount of cloudy urine filled with small gray amorphous particles. The ureters were slender and pliable and entered the urinary bladder in the usual location. The arteries and veins were not unusual.

The urinary bladder contained a small amount of cloudy urine full of gray amorphous precipitate. The mucosa was extensively and diffusely hemorrhagic.

The brain weighed 320 grams, was soft and edematous. The usual proportion of gray and white matter was present. There was marked congestion throughout. No hemorrhages were noted. The ventricles were undilated. The pituitary was not unusual. The structures at the base of the skull presented no lesions.

Gross Anatomic Diagnois.—Atelectasis of lungs, generalized, etiology uncertain, congestion of lungs, edema and hyperemia of the brain, uric acid infarcts of the kidneys, submucosal hemorrhages of urinary bladder, prematurity, icterus.

Mechanism of Death.—The mechanism of death was highly suggestive of uremia.

Microscopic Examination.—Lungs: General architecture was preserved. The alveolar walls were delicate. All the alveoli were filled with blood as were the bronchioles.

Kidneys: The glomeruli were moderately immature but were otherwise not unusual. The collecting tubules were almost all plugged with casts of granular eosinophilic material containing red blood cells, white cells, and cellular debris. The epithelium of these tubules showed both degenerative and regenerative changes. Some of the convoluted tubules contained protein casts. The blood vessels were not unusual.

Brain: There were generalized hyperemia and moderate edema.

Urinary Bladder: There was extensive recent submucosal hemorrhage. The muscle wall appeared to be hypertrophied.

Final Diagnosis.—Uric acid infarcts of kidney, extensive, hemorrhage into lungs, congestion of lungs, submucosal hemorrhages of urinary bladder, edema and hyperemia of brain, prematurity, icterus.

Stimulated by the foregoing case, the next fifteen patients who were admitted to St. Elizabeth's Hospital with toxemia of pregnancy were followed. As soon as the infant was delivered, samples of cord blood were taken and total protein, uric acid, and nonprotein nitrogen determinations were done. Seven of the fifteen cases showed a definite elevation of uric acid, and these cases make up the remainder of this report (Table I).

All the infants in this series were liveborn, and all the infants survived. Six of the seven were born at term; one was six weeks premature by date.

TABLE I. RELATION OF FETAL WEIGHT, CORD BLOOD URIC ACID, AND MATERNAL ACID

NO.	BIRTH WEIGHT	CORD URIC ACID	MATERNAL URIC ACID
1	8 pounds	7.2	6.0
2	6 pounds, 1½ ounces	6.3	6.6
3	7 pounds, 7½ ounces	7.1	4.8
4	3 pounds, 10 ounces	10.6	6.8
5	8 pounds, 1 ounce	5.2	5.2
6	6 pounds, 10½ ounces	8.6	10.0
7	6 pounds, 2 ounces	6.7	6.7

Six were born to primigravidas and one to a tertigravida.

The relation of the babies' weights to the uric acid of the cord blood is recorded in Table I. With the exception of Case 4, it will be observed that all infants are of good weight. The small infant in Case 4 survived and did very well, being discharged at a weight of 5 pounds.

Table I also shows the relation of the fetal or cord uric acid to the maternal uric acid. There is a close enough proximity in four of the cases to warrant speculation as to whether or not the nitrogenous products had not filtered through the placental barrier. The remaining three cases are difficult to evaluate. Two have an increase in the cord uric acid; one a decrease in the cord uric acid. It will be necessary in future studies to compare both the cord blood and venous blood from the infant to determine whether these products are the result of filtration of nitrogenous wastes through the placenta or actual products of metabolism of the fetus in utero. If the latter, it will then be necessary to determine whether there is a toxin in the maternal circulation which can be filtered through the placenta and into the fetal circulation, stimulating either an azotemia or, in rare cases, a definite uremia.

Summary

A case of probable uremia of the newborn is reported.

Seven other cases of probable azotemia of the newborn are presented as a preliminary report of work that is now in progress.

59 BEECH STREET

Department of Case Reports New Instruments, Etc.

HEMANGIOMA OF THE UMBILICAL CORD

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BENIGN tumors of the umbilical cord and placenta are rare, but are of considerable interest because of their pathological relationship with other complications of pregnancy and parturition. Siddall[1] in 1924 presented the first comprehensive review of this subject. He reported one instance of chorangioma of the placenta and reviewed the previously reported 130 cases. In 32 per cent of the cases polyhydramnios and premature labor developed. The mortality rate of the premature infants was 68.6 per cent in the 130 reviewed cases. The majority of the tumors were hemangiomas and were located in the placenta.

In 1939 Marchetti[2] reported eight instances of benign tumors of the placenta bringing the total number of reported cases to 217. He believes that these tumors are of interest because of the associated occurrence of dystocia and polyhydramnios.

Since Marchetti's review, there have been seventeen reported cases of benign tumors of the placenta and one angioma of the umbilical cord.[3] This makes a total of 234 benign tumors of the placenta and one of the umbilical cord. It is the opinion of the authors that the latter figure is inaccurate, for in a review of the previous case reports of tumors of the placenta, several were found that might have arisen from the umbilical cord. However, an accurate evaluation of these tumors could not be made because of incomplete reports.

This case is reported because of its unusual morphology and its association with polyhydramnios and premature labor.

B. P. (No. 8334d), a 19-year-old white girl, gravida ii, para i, was first admitted June 1, 1950, and discharged June 6, 1950. The second hospital admission was June 11, 1950, to June 19, 1950.

First Admission.—

Chief complaint: Swelling of the ankles of three days' duration.

Past history: The onset of menses occurred at the age of 16 years with periods occurring regularly every 30 to 36 days. The usual duration of flow was 6 to 8 days. There was one previous pregnancy which terminated March 20, 1948, with the normal delivery of a live full-term infant. At approximately three months' gestation of the first pregnancy, there was some albuminuria which cleared after the patient was placed on a low-salt diet. There were no other complications of the first pregnancy.

Present illness: The patient first consulted her physician three months before admission because of amenorrhea of four months' duration. The last menstrual period had been Oct. 20, 1949. The diagnosis was uterine pregnancy of four months' duration. The red cell count was 4.12 million. There were 14 Gm. hemoglobin per 100 c.c. The blood pressure was 120/70 mm. There had been a weight increase of 12 pounds over her usual 115 pounds. On examination three weeks later there was no change in blood pressure, but a 4

plus albuminuria was detected. On succeeding examinations urinalysis was normal after a low-salt diet and a urinary antiseptic had been prescribed. Three weeks before admission, a trace of albumin and several white blood cells were found on urinalysis. The blood pressure remained normal. There was no edema, but there was a weight increase of 11 pounds for a total gain of 26 pounds. One week before admission, the patient developed a urinary infection manifest by costovertebral angle pain and tenderness and a fever of 101.2° F. Urinalysis revealed 2 plus albuminuria and many white blood cells per high-power field with clumping. Bed rest, forced fluids, and antibiotics were administered and there was considerable improvement. Three days before admission the patient noted the onset of edema.

Physical examination: The patient's temperature was 98° F., pulse 94, respirations 20, and the blood pressure was 120/72 mm. The uterus was enlarged to the size of eight months' pregnancy and was very firm, making palpation of the fetal outline difficult. The fetal heart tones were heard in the left lower quadrant of the abdomen. There was 2 plus pitting edema of the lower extremities. External pelvic measurements were normal.

Laboratory data: The nonprotein nitrogen was 22 mg. per cent. The blood urea nitrogen was 4.7 mg. per cent. There were 3,640,000 red blood cells and 9,200 white cells per c.mm. The hemoglobin was 10 Gm. per 100 c.c. of blood. There was 2 plus albuminuria.

Course in hospital: The patient was placed on bed rest, salt-free diet and ammonium chloride. It was the opinion of a consultant that there were hydramnios and nephritis complicating pregnancy, and conservative management was recommended. The edema subsided, but there was a persistent 1 plus albuminuria. The patient was discharged on the fifth hospital day and placed on a low-salt diet.

Second Admission.—

Five days later, with the onset of labor pains one hour before admission. The patient had not felt any fetal movement for three days. The membranes had not ruptured. The patient's temperature was 99.8° F., pulse 80, respirations 20, and the blood pressure was 118/70 mm. The patient was in active labor, the uterine contractions occurring every three to four minutes, lasting 30 to 45 seconds. The uterus was symmetrically enlarged. The top of the fundus was 32 cm. above the symphysis pubis. The fetal outline was ill defined. Fetal heart tones were not heard. Rectal examination disclosed a 2 cm. dilated, completely effaced, soft cervix. The presenting part was at the level of the ischial spines. The membranes were not ruptured. There was 2 plus pitting edema of the lower extremities.

Course in the hospital: The first stage of labor lasted six hours and forty minutes. The patient received Delvinal Sodium, 7 grains intravenously, and 100 mg. of Demerol intramuscularly, with adequate analgesia. When the cervix was 5 cm. dilated, the membranes ruptured spontaneously with loss of an estimated 1,000 c.c. of amniotic fluid. After a brief second stage, the patient was easily delivered of a living premature male infant. At this time an estimated 4,000 c.c. of amniotic fluid were expelled. The placenta was spontaneously delivered after a short third stage. A large tumor was attached to the umbilical cord near the placenta. Respirations in the infant were established with difficulty and he was placed in an incubator. Oxygen and stimulants were administered, but he expired ten hours after birth. Postmortem examination was performed and the pathologic diagnoses were: incomplete division of the truncus arteriosus with right aortic arch, hypoplasia of the ascending aorta; hypertrophy and dilatation of the heart, most advanced on the right; and cavernous hemangioma of the liver.

The postpartum hospital course of the mother was uneventful. Urinalysis showed a persistent 1 to 2 plus albumin and a few white blood cells per high-power field. The blood pressure remained normal and the patient was discharged on the seventh postpartum day.

Subsequent course: Examination four weeks after discharge showed normal blood pressure, weight, and urinalysis. The patient returned two months later with vague urinary symptoms. Chemical examination of the urine revealed 2 plus albuminuria. Intravenous

pyelography was normal. The nonprotein nitrogen, urea nitrogen, creatinine, and uric acid determinations were normal. Numerous subsequent examinations of the urine have disclosed no albumin.

Fig. 1.

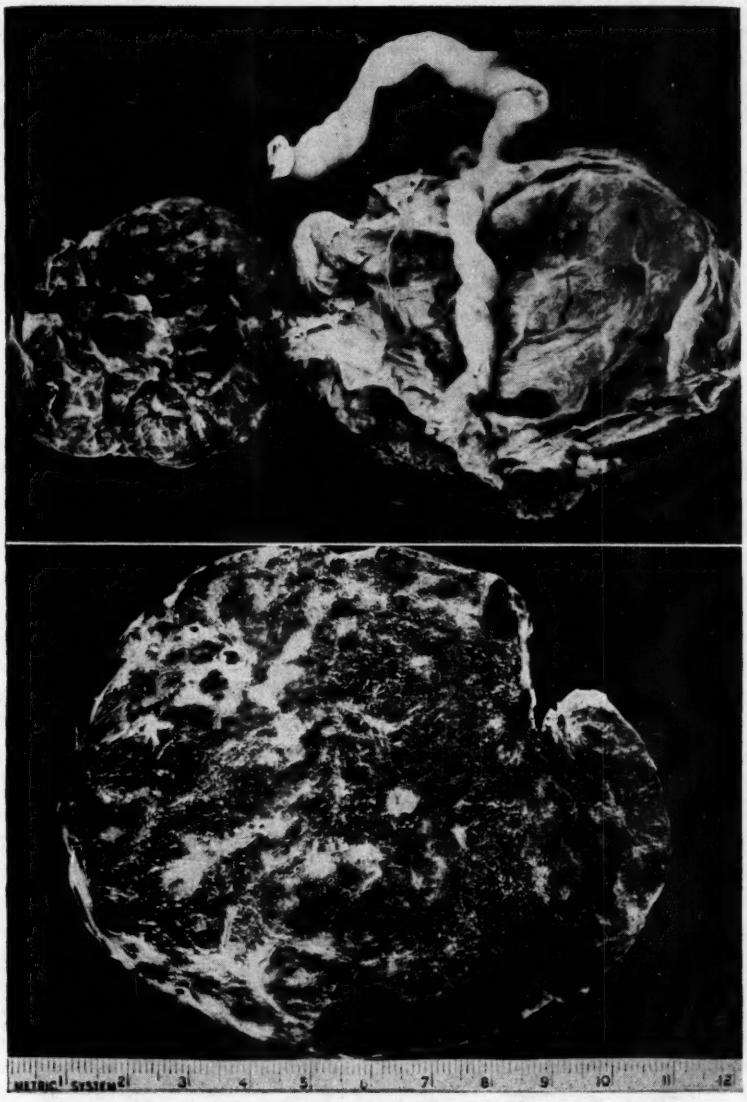

Fig. 2.

Fig. 1.—Gross appearance of tumor and fetal surface of placenta showing distinct pedicle attaching tumor to umbilical cord.

Fig. 2.—Cut surface of tumor. Note lobulated appearance with angiomatous tissue separated by interlacing fibrous connective tissue.

Pathological Report.—

Gross: The specimen consists of a placenta measuring 20 by 18 by 6 cm. The attached umbilical cord measures 30 cm. in length and is 3 cm. in its greatest diameter. There is a reddish-blue, firm mass, measuring 10 by 12 by 8 cm. attached to the umbilical cord 5 cm. from the insertion of the latter into the placenta. The tumor pedicle is 8 cm. in length (Fig. 1). The tumor appears completely encapsulated by a thin, shiny membrane. The cut surface

of the tumor presents a lobulated appearance. There is an abundance of moderately firm, reddish-blue tissue divided irregularly by deposits of interlacing fibrous connective tissue (Fig. 2). Large amounts of bloody fluid are expressed from the cut surface. Multiple sections through the placenta show many scattered zones of hemorrhage. There is no evidence of tumor within the placenta.

Microscopic: Sections of the tumor show numerous vascular spaces, many of which are dilated and filled with intact red blood cells. In some regions, there is proliferation of

Fig. 3.

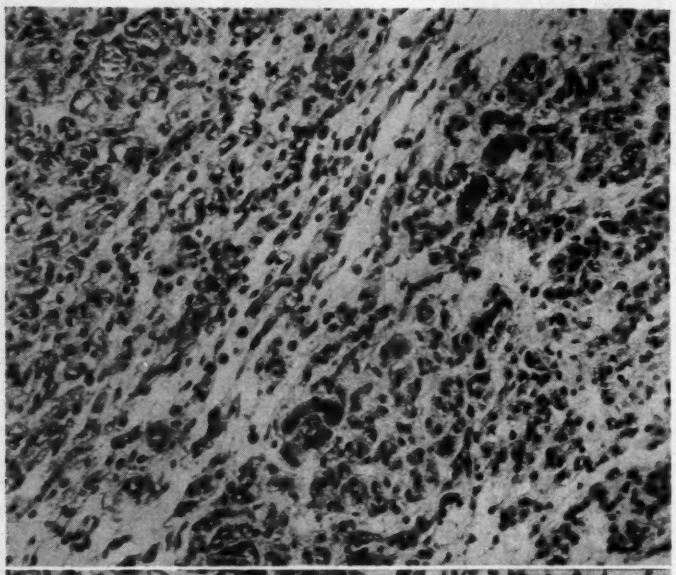

Fig. 4.

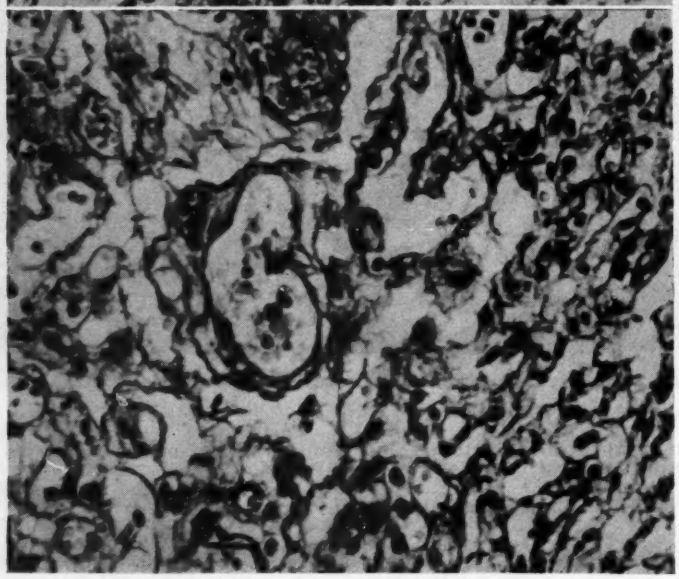

Fig. 3.—Microscopic appearance. Note numerous vascular spaces separated by loosely arranged connective tissue. (Hematoxylin and eosin. ×70.)

Fig. 4.—Microscopic appearance. The vascular spaces are sharply outlined as a result of impregnation of endothelial cells with silver. (Wilder silver impregnation for reticulum. ×430.)

endothelial cells without formation of well-developed vascular channels. The vessels are supported on a loosely arranged stroma of myxomatous connective tissue (Fig. 3). There is an intact capsule at the periphery. The nuclear pattern of the endothelial cells is constant. There is no evidence of pathologic mitotic figures or invasive tendency. There is no extension into the vascular channels. Sections from various regions show no evidence of chorionic elements.

Wilder silver impregnation for reticulum: The cells lining the vessel wall are deeply impregnated with silver by this method which sharply outlines the vascular spaces. The endothelium lining the vascular channels is a single layer in thickness (Fig. 4). The surrounding supporting tissue contains no reticulum.

Masson trichrome stain: The supporting substance stains deeply green indicating its connective-tissue origin. The endothelium lining the vascular channels is a single layer in thickness and stains a pale reddish blue.

Sections of the placenta show numerous mature chorionic villi lined by a single layer of syncytial cells and containing mature blood vessels in the core of the villus. There are numerous regions of recent hemorrhage.

Diagnosis.—Hemangioma of the umbilical cord.

Comment

The pathogenesis of benign tumors of the placenta and umbilical cord has aroused considerable interest. In 1898 Albert[4] proposed a theory that in early embryonic development a blood vessel could occasionally branch off from that portion of the allantois and chorion which fuse into the umbilical cord. Failing to find a normal association, this vessel could independently form a hemangiomatous tumor. However, this theory was refuted in 1905 by Schickele,[5] who established that the blood vessels of the chorionic villus develop in situ. Siddall[1] concluded that the preponderance of evidence was in favor of development from a single villus. Marchetti[2] felt that "the resemblance of the components of chorioangioma to the blood vessels and stroma of the normally developing chorionic villus unquestionably points to their origin from the chorionic mesenchyme, the common source of endothelial and connective tissue."

Albert[4] reported an angioma separate from the placenta and completely encapsulated. The tumor rested against the edge of the placenta, but was not attached to it. There was a large artery entering one side and a large vein leaving from the opposite surface of the tumor. These vascular channels arose from the umbilical cord at its insertion into the placenta and coursed over the fetal surface of the placenta giving off many branches before entering the tumor. Such a lesion is much more intimately associated with the placenta than that reported in this paper, but still could have arisen from the umbilical cord.

In considering the pathogenesis of the tumor reported in this paper several characteristics which distinguish this tumor from those previously recorded must be kept in mind. The first is that this tumor was completely separate from the placenta, attached by a highly developed vascular pedicle to the umbilical cord. The second important consideration is that thorough microscopic study of numerous sections taken from various portions of the tumor fail to reveal any chorionic elements. There are two possible explanations of the origin of such a tumor. First, an accessory placenta might develop an angioma. With continued growth, such a lesion could possibly completely replace the accessory lobe, leaving a benign, encapsulated tumor attached by a pedicle to the umbilical cord. What was previously an umbilical cord to an accessory placenta would become the tumor pedicle. However, it seems unlikely to the authors that a benign tumor of this type could so completely replace the succenturiate lobe that no remnant of placental tissue could be found on microscopic study.

The other possible explanation is that this tumor represents a true neoplasm of the umbilical cord. We believe that such a theory best explains this lesion. The findings of a benign, encapsulated tumor of endothelial cells devoid of chorionic elements, attached by a well-developed pedicle to the umbilical cord are all consistent with a true neoplasm

arising from the vascular channels of the umbilical cord. Since we do not know the time of onset of development of the tumor and because the lesion had attained considerable size, the diagnosis of hamartoma is not justified. The size of the tumor plus the microscopic appearance force a diagnosis of true neoplasm until proved otherwise. The location and gross and microscopic characteristics make development from the umbilical vessels the most likely theory of origin.

Clinically this case supports Siddall's finding of a high incidence of polyhydramnios and the associated complications of premature labor and high fetal mortality. It is unlikely that the pyelonephritis present in this patient was related to the hydramnios or premature labor. Although the findings on postmortem examination of the infant preclude life, this does not detract from the fact that this tumor was definitely associated with polyhydramnios and premature delivery.

Although there was no dystocia, a lesion of this type, with its own pedicle and in the presence of increased amniotic fluid, could easily enter the birth canal before or with the infant. This could produce a dystocia and several such cases are on record. One was preoperatively diagnosed as placenta previa and treated by cesarean section.[6] Another was dislodged manually and followed with a forceps delivery.[7] It would seem advisable to keep this unusual lesion in consideration as a possible cause of dystocia, particularly in the presence of polyhydramnios. Obviously the tumor cannot be diagnosed until the time of delivery. The improved care of premature infants will decrease the infant mortality associated with these tumors. Since all reported tumors of this type have been benign, their main importance is that they are commonly associated with hydramnios and premature delivery and are rarely a cause of dystocia.

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CONCOMITANT ENDOMETRIOSIS AND CARCINOMA OF THE RECTOSIGMOID*

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THE paucity of reported cases of endometriosis of the rectosigmoid concomitant with carcinoma of the rectosigmoid is probably not indicative of the frequency with which these lesions coexist. Accounts can be found of carcinoma arising in the ectopic endometrial tissue in the pelvis and colon; spindle-cell sarcoma of the rectum containing endometrial tissue has been reported.[1] Braine cited a case of rectal cancer concomitant with a stenosing rectosigmoidal endometrioma treated by abdominoperineal resection.[2] Jose and Hanson have described a case of carcinoma of the sigmoid associated with endometriosis in the pelvic pouch.[3]

Since 8 to 15 per cent of all women during active menstrual life have endometriosis and of these approximately 25 per cent have involvement of the rectosigmoid, it has been estimated that 2 to 4 per cent of all women during active menstrual life have rectosigmoidal endometrial invasion of some degree.[4] Although endometriosis is most common between the age of 30 and the menopause, Haydon reported a case at age 16 and another at age 78.[5] Carcinoma of the rectosigmoid has been described at all ages between these extremes. It is therefore not surprising that the two conditions should coexist. The management of such cases presents interesting problems, as illustrated by the following report.

The patient, A. Y., a 51-year-old white housewife, was first studied in 1936 for complaints of shortness of breath, excessive gas, belching, constipation, fatigue, and nervousness, which were exaggerated immediately before and after the onset of menstruation. Mucus and, occasionally, bright red blood were passed with stools. Her menstrual periods were regular. A right nephrectomy had been performed 12 years previously for nephrolithiasis. Physical examination revealed a nervous, apprehensive individual with subacute follicular tonsillitis, and slight fullness over the thyroid gland; the heart and blood pressure were normal. No abdominal tenderness, masses, or visceral enlargement were present. Examination of rectum, however, elicited marked tenderness. Sigmoidoscopy revealed no mucus nor blood, but the mucosa was definitely congested with the suspicion of slight pigmentation in the lower sigmoid, but no suggestion of melanosis. A small internal hemorrhoid and questionable cryptitis were additional findings.

Laboratory Data.—Blood count: Hemoglobin 14 Gm., white blood cells 7,600, polymorphonuclear leucocytes 76 per cent, lymphocytes 24 per cent. Urine: normal. Wassermann: negative. Van den Bergh: 0.2 per cent bilirubin. Cholesterol: 180 mg. per cent. Basal metabolism rate: plus 6. Gastric analysis: free acid 10 units, total acid 15 units. Feces: brown, semiliquid, occult blood plus 3. A barium enema x-ray study showed a tortuous colon with diverticuli in the lower descending and pelvic bowel. The entire colon showed a profound degree of spasticity and irritability.

A regimen for treatment of the diverticulosis was advised and she was returned to her private physician.

During the next 12 years this patient had two bowel movements a day which were normal in color and character. In August, 1948, the stools became softer, but not watery; they again contained mucus and later blood. Since her previous hospitalization she had

*Presented at a meeting of the Philadelphia Obstetrical Society, Dec. 8, 1950.

gained 12 pounds. Physical examination now revealed a blood pressure of 240/130; the heart was enlarged to the left and a systolic apical murmur was heard. The abdominal findings were significant: she had a large tumor in the hypogastrium, approximately 8 cm. in diameter, which was hard, fixed, and seemed to be in relation to another tubelike structure coming from the right margin of the first mass and extending laterally up toward the anterior superior spine of the right ilium. This tumor was also fixed; neither mass was tender. Abdominal pressure on the tumors could not be transmitted to a finger within the rectum. A rock-hard mass was palpated in the cul-de-sac making pressure on the rectosigmoid. At a depth of four inches a benign-appearing polyp was visualized through the sigmoidoscope. Another similar lesion was seen at eight inches. Biopsies of these polyps were reported as benign.

Hospitalization was arranged and addiitonal studies revealed a Grade 2 hypertensive retinopathy; an electrocardiogram showed a few changes consistent with hypertensive cardiovascular disease but no clinical evidence of heart failure existed. The gynecological consultant confirmed the large pelvic mass and he expressed the opinion that the tumor was most likely a uterine myoma but that the possibility of an ovarian cyst could not be ruled out. A persistent nonobstructing defect in the lower pelvic colon was seen by barium enema but in view of the pelvic mass this defect was thought to be extrinsic in nature.

Laboratory Data.—Blood count: red blood cells 4.26 million, hemoglobin 12.5 Gm., white blood cells 6,000, polymorphonuclear leucocytes 55 per cent, lymphocytes 42 per cent, eosinophiles, 3 per cent. Urinalysis: Specific gravity 1.025, albumin trace, sugar negative, 2 to 5 white blood cells per high-power field. Sedimentation rate: 30 mm. Feces: occult blood negative. Blood urea nitrogen: 14 mg. per cent. Serum bilirubin: 0.2 mg. per cent. Alkaline phosphatase: 1.1 Bodanski units.

Laparotomy was performed Jan. 3, 1949. A myomatous uterus the size of a four months' pregnancy and a large endometrial cyst involving the right ovary were exposed. The endometrioma was situated posterior to the large uterine tumor and was densely adherent to the midsigmoid. The cyst was freed from the bowel by sharp and blunt dissection and was removed with the uterus and both ovaries. The outer wall of the sigmoid was densely indurated and was obviously invaded by endometrial implants at the site of attachment of the endometrioma; this was the same area of deformity depicted in the barium enema study. It seemed plausible that this region of induration in the sigmoid represented an invasion of the endometrioma. However, on palpation one had the impression that an intraluminal tumor was present. The tumor was in the mesenteric side and occupied over one-half the circumference of the bowel. The mesentery was thickened as a result of the endometriosis, making the search for mesenteric glands difficult. Since it was definitely known that two adenomatous polyps were present in the rectum and sigmoid, a search was made for other similar lesions. Palpation of the colon disclosed a large pendunculated polyp in the upper sigmoid 12.5 cm. above the tumor in the midsigmoid. The rectal polyp could not be palpated nor others in the remaining colon. Inadequate bowel cleansing, however, hampered the examination.

The indurated area was exposed through a small incision in the longitudinal band of the sigmoid; the mucosal lesion was so characteristic of malignancy that resection was imperative. No glands were palpated in the mesentery of the sigmoid nor along the inferior mesenteric artery. There was no evidence of metastasis to the liver. The rectal polyp previously observed on sigmoidoscopic examination was not palpable. The proximal third of the rectum and the entire sigmoid colon were resected; on inspection of the resected specimen it was found that the sessile polyp extended almost to the lower edge of the rectal segment. An additional 2 cm. of rectum were then excised and an end-to-end anastomosis was performed between the lower half of the rectum and the descending colon.

The pathologist reported multiple leiomyomas in the uterus. Diffuse endometrial invasion was observed in the Fallopian tubes and ovaries and about the cyst. In one adenomatous polyp there was mucoid carcinoma in the pedicle and in the adjacent wall of

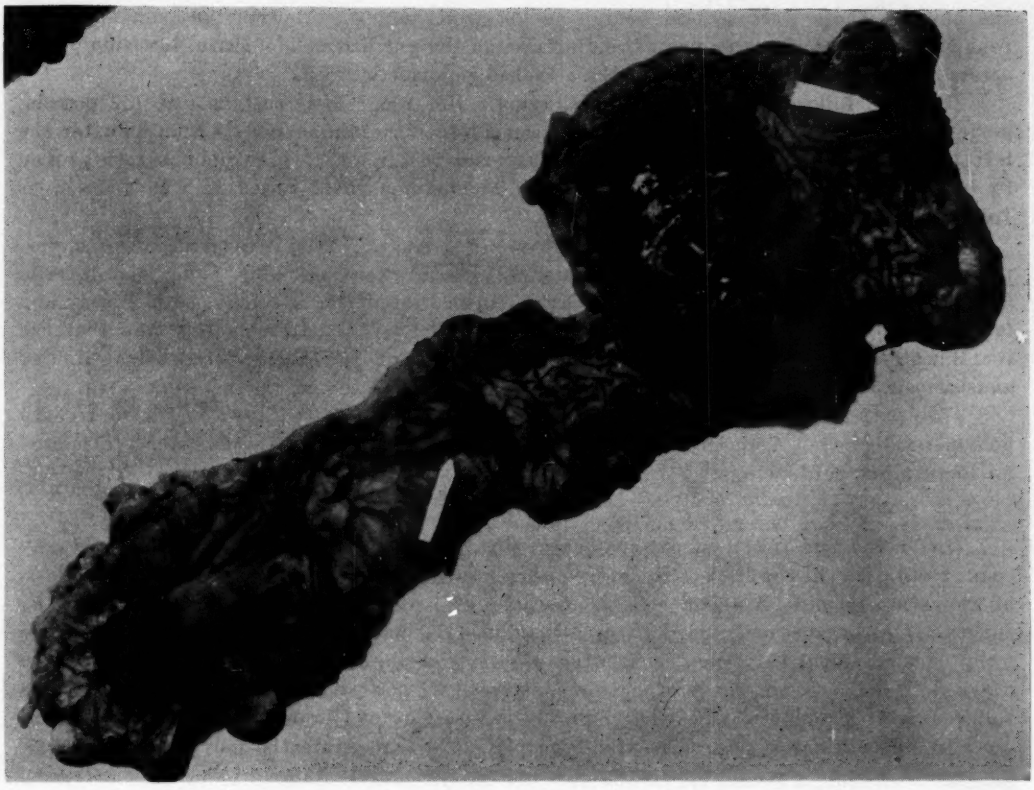

Fig. 1.—The lumen shows pedunculated polyps and carcinoma. More of the proximal rectum was resected due to nearness of polyps to the transection line.

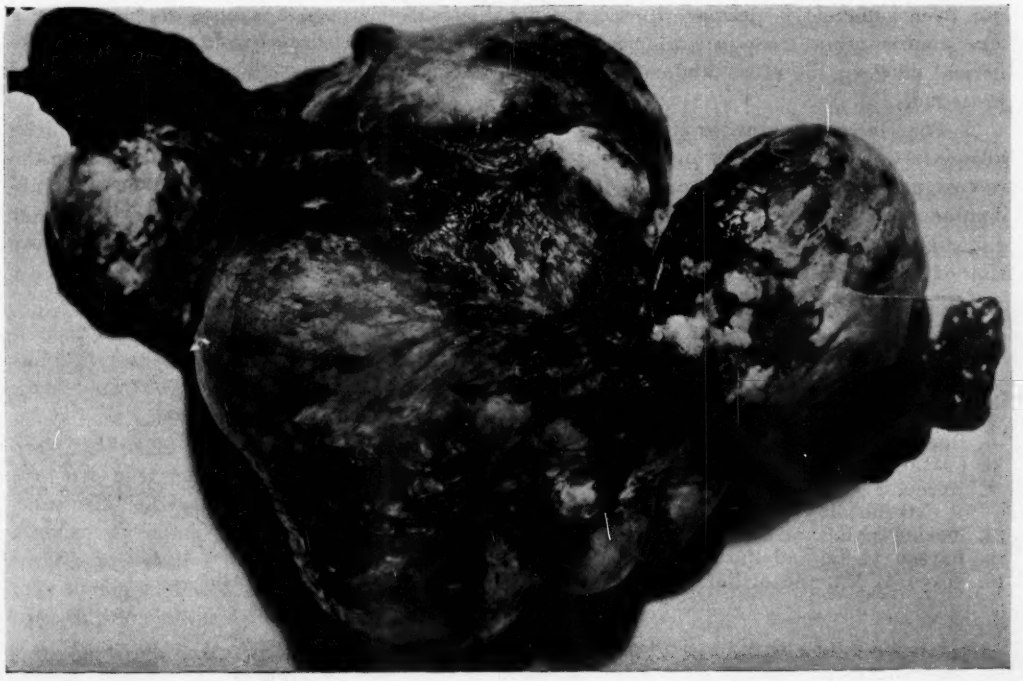

Fig. 2.—Fibroid tumors of uterus and large endometrioma involving right ovary. Endometrial transplants on peritoneal surfaces of specimen.

the bowel. There were several benign adenomatous polyps. Another polypoid mass was found to be a mucoid carcinoma extending around the gut, with endometrial invasion of the serosa and muscularis, at the site of the attached endometrial cyst.

Periodic follow-up visits were encouraging. Her weight was sustained at 152 pounds; her appetite remained good. However, a sigmoidoscopic examination six months after she left the hospital disclosed a polyp on the anterior rectal wall, which upon biopsy proved to be adenocarcinoma. Readmission for an abdominoperineal resection was advised as fulguration did not seem adequate.

An abdominoperineal resection was performed Aug. 1, 1949. No evidence of metastasis was present in the liver. No enlarged glands were palpable along the inferior mesenteric artery nor along the aortic chain. Inspection of the specimen both grossly and later microscopically showed that the base of the polyp was carcinomatous and that the rectal wall was invaded. A new sessile polyp was found just below the previous line of anastomosis. Several smaller smooth polyps could be detected in the same area.

The patient made an uneventful convalescence and was dischraged on the fourteenth postoperative day. A recent barium enema study made through the colostomy disclosed no further polypoid change.

Comment

Endometriosis of the colon and rectum simulates carcinoma in some respects and may coexist with it. In the literature conservative treatment of minor degrees of endometriosis of the rectosigmoid has been stressed because of a desire to preserve the childbearing function and because only one-half of all endometrial lesions of the rectosigmoid produce symptoms. Radical treatment, consisting of bilateral oophorectomy, or irradiation of the ovaries, is indicated in cases of greater involvement, as cessation of ovarian function is followed by regression of the lesion. Rarely is resection of the involved bowel indicated.[1]

In this patient it had originally been planned to fulgurate the polyps, demonstrated by sigmoidoscopic examination, after removal of the pelvic tumor. The circumscribing carcinoma beneath the endometrial invasion of the sigmoid could easily have been mistaken for endoemtrial invasion alone if the colon had not been opened. Direct inspection of the lesion disclosed that resection was mandatory. Unfortunately, the remaining colon had not been sufficiently cleansed for accurate palpation. Through the open rectum nothing was visible other than several small, smooth, rounded plaques covered with apparently normal mucosa; therefore, abdominoperineal resection did not seem justified at the original procedure.

Four lessons are apparent. As polyps are likely to be multiple, the bowel should be adequately prepared before operation to facilitate their discovery. If a lesion is near the rectosigmoid, the patient must be mentally prepared preoperatively for a possible abdominoperineal resection and a permanent colostomy. If the surgeon cannot be sure that endometrial invasion does not account for the entire sigmoidal induration, open inspection of the bowel is imperative.

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PERITONEAL GRANULOMA SECONDARY TO RUPTURED DERMOID CYST

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THE rupture of a benign dermoid cyst of the ovary is relatively uncommon. The granulomatous (peritoneal) reaction set up by the liberated sebaceous material, on gross examination, may easily be mistaken for tuberculous peritonitis. It was felt, therefore, that the present case would merit publication.

The patient was a 25-year-old gravida i, para i, with a history of sudden, severe lower abdominal pain at 7 months' pregnancy. During the following week the pain recurred at intervals but was less severe and the patient went on to normal delivery of a 7-pound male child on March 3, 1950. Routine postpartum examination revealed no abnormalities.

Six months later the patient was seen again and presented the following symptoms which she dated for the most part as following closely upon the birth of her child. The patient experienced a general feeling of fatigue, irregular bowel habit, with small, hard stools, frequency of micturition, and a feeling of fullness in the lower abdomen. In addition she stated that for the previous five weeks she had noticed a mass in the lower abdomen which had been increasing in size but was not tender unless accidentally bumped.

Examination revealed a moderately hard, somewhat elastic mass, most prominent in the lower right side of the abdomen. It was freely movable and measured approximately 8 inches across and extended from the symphysis to just below the umbilicus. Catheterization revealed no change in size and shape of the mass. Laboratory examination, aside from a slightly lowered hemoglobin estimation, revealed no significant abnormalities. A diagnosis of a rapidly growing ovarian cyst was made and operation advised.

The abdomen was explored through a midline suprapubic incision, and a left ovarian cyst measuring 8 inches in diameter and a right ovarian cyst measuring 3 inches in diameter were removed. From the the pouch of Douglas a free mass of hair and sebaceous material surrounded by a fibrous capsule was removed. Scattered over the peritoneum and the omentum numerous small yellowish-white nodules measuring 0.2 to 0.4 cm. were seen, which somewhat resembled a tuberculous peritonitis. Specimens were taken for pathological examination, and were reported as follows:

"Specimen consists of a large multiloculated cyst measuring 25 by 15 cm. and contains a clear slightly gelatinous fluid. In one area there is some calcareous deposit and a definte tooth structure. The second portion of this specimen consists of a cyst measuring 5 cm. in diameter. It contains a large amount of yellowish clear liquid fat and a large hair ball. The ovary is in one wall of this cyst and a small corpus luteum cyst is present.

"Sections from the left ovary show a large cyst lined by a single layer of goblet cells. The stroma is fibrous in type. In another area, a cyst can be seen which is lined by stratified squamous cell epithelium with numerous sebaceous glands, hair follicles, and apocrine sweat glands. In one area, hyaline cartilage and bone tissue can also be seen. Sections from the right ovary show cyst lined by stratified squamous cell epithelium with sebaceous glands and hair follicles. There are also sweat-gland-like structures in the depth. Normal ovarian stroma with follicle cysts can also be seen and one corpus luteum."

Diagnosis: 1. Benign teratoma of right ovary. 2. Benign teratoma and pseudomucinous cystadenoma of left ovary.

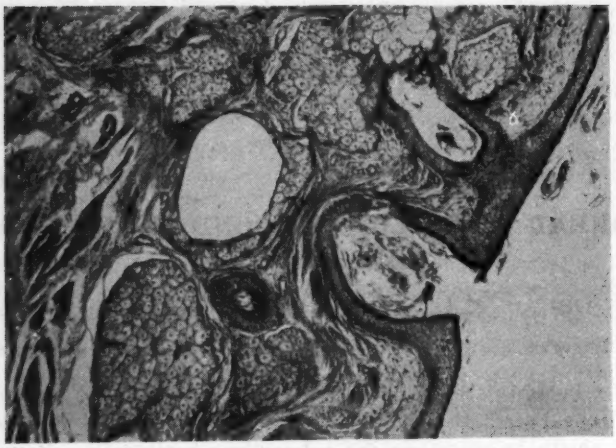

Fig. 1.—Section of tumor in right ovary. (×54.)

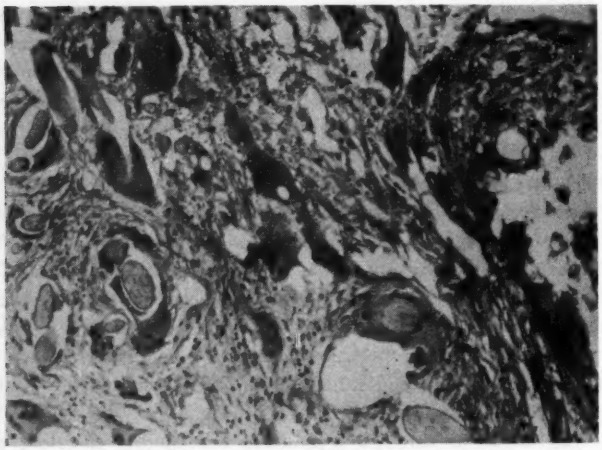

Fig. 2.—Section from mass in pouch of Douglas. (×128.)

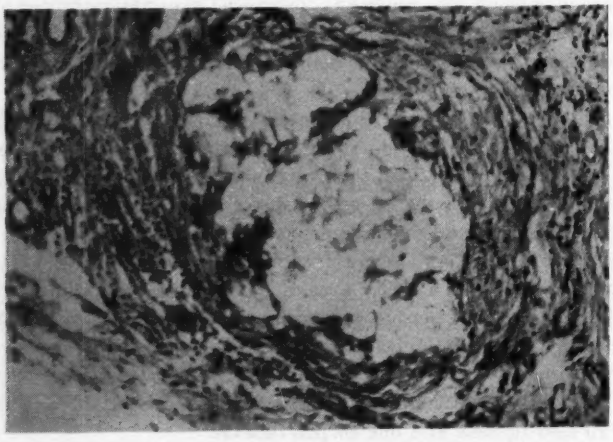

Fig. 3.—Section from peritoneal granuloma. (×128.)

"Specimen 2 consists of a small piece of serous membrane associated with numerous small yellowish-white calcareous bodies measuring approximately from 0.2 cm. to 0.4 cm. in diameter.

"Section shows granuloma composed of macrophages, some of which are lipoid laden. There are also a few foreign body giant cells. The granulomatous reaction can be seen surrounding the space which contains some debris and out of which some material has been dissolved by the dehydrating process. No crystals can be seen. There is no evidence of tuberculosis. The material responsible for the reaction was most likely sebaceous material extruded from ovarian cysts. Fat stains of frozen sections showed presence of neutral fat in the centre of the granulomata."

Diagnosis: Foreign body granuloma.

Section from the mass in the pouch of Douglas revealed sebaceous material and hair surrounded by fibrous tissue with an intense granulomatous reaction. There was no epithelial lining present.

Comment.—A review of the literature reveals this to be the fifth such case to be reported and the second to mention the peritoneal granuloma caused by such a rupture. The possibility of confusing the diagnosis with a tuberculous peritonitis has been pointed out.

Acknowledgment.—We wish to thank Dr. J. L. Hall for permission to publish this case.

UTERINE ADENOCARCINOMA IN A PATIENT RECEIVING ESTROGENS

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STILBESTROL has come into extremely wide usage as an inexpensive and effective means of treating the vasomotor symptoms of the menopause. Like estrogens in general, excessive amounts may produce a hyperplasia of the endometrium, and although most of these cases are easily recognizable as such, more complex hyperactive forms can be found in which the microscopic resemblance to adenocarcinoma is a real one.

As yet there is no evidence that estrogens produce genuine fundal adenocarcinoma. Many gynecologists, however, accept some possible relationship between the postmenopausal types of hyperplasia and the later development of uterine cancer, and, if we know that atypical hyperactive forms of hyperplasia can be produced by estrogens, it behooves us to be cautious in our use of the drug.

Adenocarcinoma of the fundus is a common type of tumor and it should not be surprising if a certain number of the many women receiving estrogens should develop the disease. Nevertheless, the potential stimulating action of estrogens should be kept in mind, and the drug should be used in the most limited amount feasible. The following brief case report concerns a woman whose estrogen therapy was of just the opposite sort.

CASE 1.—(Bon Secours Hospital No. 76862.) This was a 60-year-old spinster who was first seen July 12, 1950, because of irregular bleeding. She began taking stilbestrol twelve years ago, on the prescription of her family doctor, because of nervousness, fatigue, and hot flushes. Throughout the years she continued to take a 1 mg. tablet nightly, and had continued to have bleeding at intervals throughout those years. For about the last five years the bleeding was scantier but there was always an interval of approximately 20 to 30 days. A week before being seen she began to flow profusely.

Examination was difficult because of the intact hymen and extreme nervousness, but an irregularly enlarged myomatous uterus was present. The usual dilatation and curettage were not performed because it was felt that the large myomas mandated a hysterectomy and that an intact specimen was preferable, if it could be obtained without jeopardizing the patient. Accordingly a total abdominal hysterectomy, bilateral salpingo-oophorectomy, and appendectomy were done July 14.

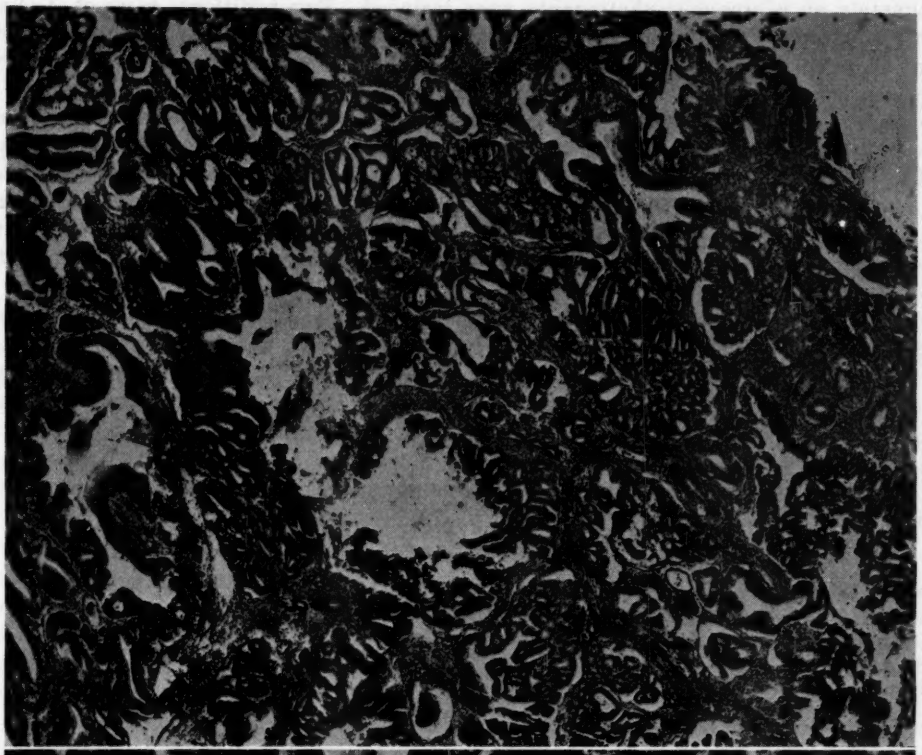
Grossly, the uterus was irregularly enlarged to about four times its normal size and revealed many characteristic myomas. There was marked hypertrophy of the myometrium and the wall of the uterus was nearly two inches thick, softened, and congested. The endometrium was likewise thick, and in addition many polyps were present, one of which was 3 to 4 cm., of the sessile type, with ulceration of its tip.

Microscopically there was both a hyperplasia and hypertrophy of the myometrium. The endometrium showed all gradations from a simple cystic hyperplasia through more complex proliferative forms (Fig. 1). High power through some of these adenomatous foci revealed a pattern which most observers would interpret as Grade 1 adenocarcinoma (Fig. 2). The ovaries were senile and atrophic.

Comment

In view of the common abuse of the estrogens, especially stilbestrol, and the frequency of adenocarcinoma of the endometrium, it would be surprising if the two did not occasionally coexist. However, there have been very few cases published as to this sequence. The case

Fig. 1.



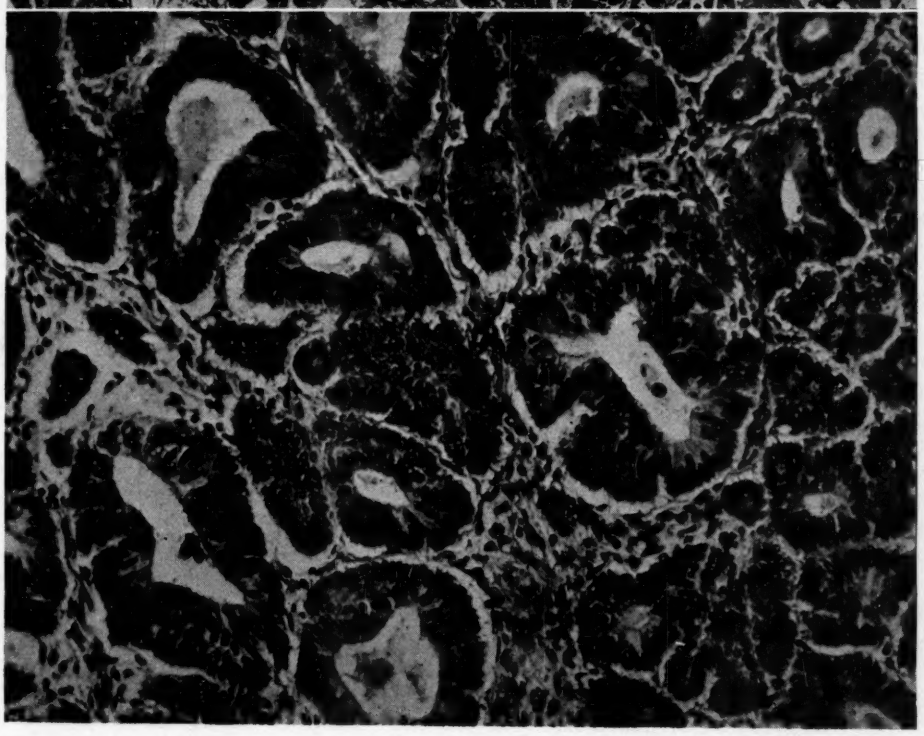


Fig. 2.

of Fremont-Smith and others certainly appears to be a bona fide instance, although unfortunately no microscopic photographs were included. Two additional cases of A. Vass,[2] with photographs, reveal what many would call a proliferative hyperplasia, although one of them is rather suspicious of early malignancy. Gusberg[3] reports five other patients who developed adenocarcinoma after estrogen therapy, and his excellent photomicrographs are strongly suggestive. Six definite cases and one probable one have been presented by Speert,[4] in which there is a long-standing history of estrogen therapy with later development of adenocarcinoma. His photomicrographs seem to confirm this. He also lists other cases reported by Henry, Riesco Undurrago, and an additional case by Fremont-Smith and Graham. Kimbrough and Muckle[5] have reported two additional cases (without pictures) in which they are "suspicious" as to the role of previous estrogen therapy in the later development of fundal adenocarcinoma.

The number of such cases is growing, and to the list another is added. If enough such instances can be accumulated, they will certainly serve as at least circumstantial evidence. At the present time we cannot indict estrogens as carcinogenic, but it is suggested that they be used cautiously, especially in patients whose family history suggests a predisposition to malignancy. In such susceptible patients we might expect a minimal stimulus to be the igniting spark, although we continue to remain ignorant as to the exact chain of reactions set up. Judicious discrimination and caution in the usage of estrogens should be observed by all.

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TUBAL PREGNANCY COMPLICATING TUBERCULOUS SALPINGITIS

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CASES of coexisting tubal pregnancy and tuberculous salpingitis have been reported from time to time. Bland[1] in 1940 cited 32 cases in an exhaustive study of the literature and added a case of his own. Since that time eight additional cases have been reported.[2-9] More cases would come to light if all tubal prenancies were studied microscopically.

Of 179 tubal gestations and 17 patients with tuberculous salpingitis seen in the past 10 years at the two hospitals where the author is affiliated, the case reported here is the only one with coexistence of tubal pregnancy and tuberculous salpingitis.

G. M., aged 29 years, para o, gravida i, was admitted to the hospital on Aug. 29, 1950, with the chief complaint of abdominal pain. She is a graduate nurse. Her last menstrual period was July 1, 1950. For two weeks prior to admission the patient noted persistent scanty vaginal bleeding. On Aug. 25, 1950, she noted the sudden onset of sharp stabbing generalized lower abdominal pain, most severe in the left lower quadrant. This subsided to a dull ache after twelve hours, when the author was consulted. Examination showed a nulliparous outlet and a normal cervix. The fundus was of normal size, forward and fixed in position, apparently by an ill-defined semisolid, moderately tender left adnexal mass. The right adnexa were normal.

A Hogben test was found positive on Aug. 29, 1950, by which time the patient's condition had improved. Repeat pelvic examination at this time was essentially unchanged. Three hours later the patient was admitted to the hospital because of a recurrence of excruciating left lower quadrant pain.

Menstrual History.—Menarche was at 11 years, periods were regular every 28 to 30 days, lasting 4 to 5 days with a normal flow. She had been infertile during a previous five-year marriage. She married again in May, 1950.

Past Medical History.—She had had an appendectomy in 1941 and a tonsillectomy in 1943. She was hospitalized because of pyelitis in 1946 and again in 1949. Each time, because of a family history of tuberculosis and because of an old minimal healed, calcified tuberculous lesion in the left upper lobe, first found in 1943, the urine was cultured for tubercle bacilli and found to be negative.

Family History.—Her father died in 1937 of pulmonary tuberculosis in a sanatorium. Her present husband had an uncle with whom the patient had occasional social contact during the previous year in a sanatorium where he was confined with far-advanced tuberculosis.

Physical Examination.—The patient obviously suffered from acute abdominal pain. Tenderness was marked in the left lower quadrant. A well-healed right McBurney scar was noted. Temperature was 97.4° F. pulse 60, respiration 20, and blood pressure 100/72.

Pelvic examination on admission was essentially as on the original examination, except that the left adnexal mass was now 10 cm. in diameter and clearly outlined. It was soft in consistency but not fluctuant. The cul-de-sac was not abnormal.

Laboratory Studies.—Blood Count: 11.5 Gm. hemoglobin, 3,790,000 red blood cells, 10,500 white blood cells, sedimentation rate 53 mm. in one hour. Urinalysis; albumin 0, sugar trace, 4 to 6 white blood cells per high-power field, occasional hyaline casts.

Operation.—a large quantity of old and fresh blood was found largely confined to the left lower quadrant of the abdomen. The left tube was found to be prolapsed behind and adherent to the left broad ligament. It was two to three times the normal diameter in its entire length. Covering the fimbria were adherent blood clots beneath which fresh blood welled

up. The right tube and ovary were involved in an old inflammatory process but were not adherent to surrounding structures. The uterus appeared normal. The left ovary could not be identified. A left salpingectomy was performed and the abdomen was closed in layers.

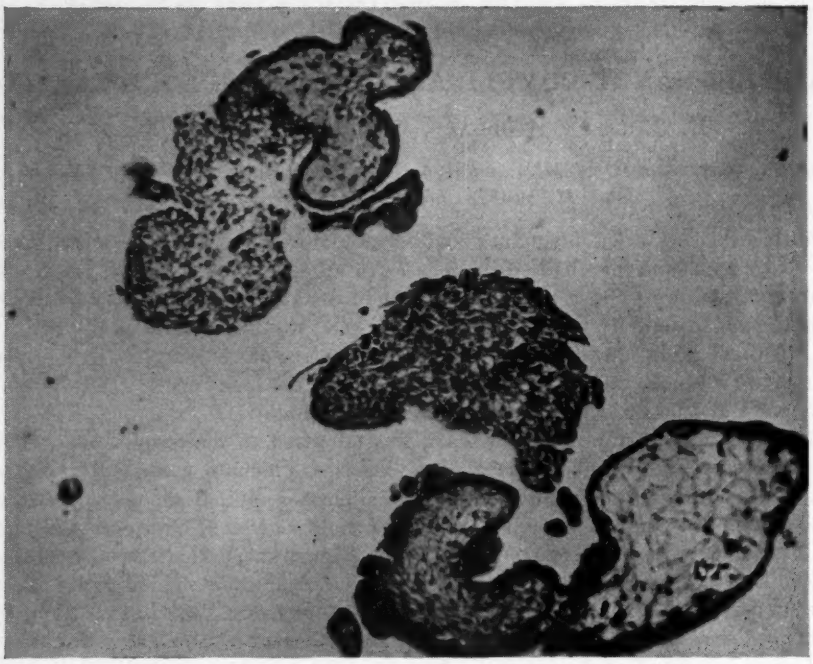

Fig. 1.—Section of blood clot removed from fimbria showing chorionic villi.

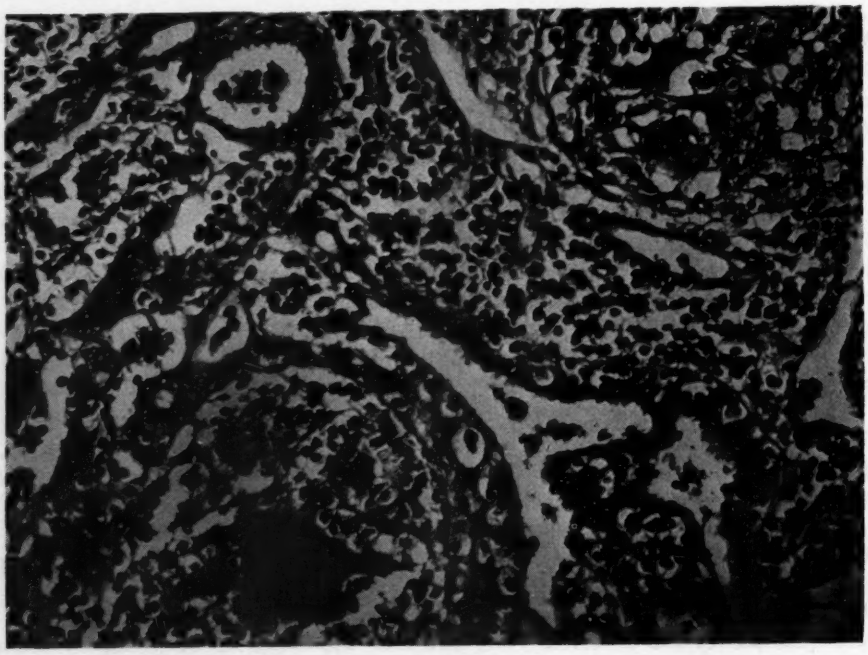

Fig. 2.—Section of Fallopian tube showing tuberculous giant cell and whorled masses of epithelioid cells.

Pathology Report.—"Sections of the blood clot which accompanied the specimen show that incorporated within the clot are many fibrotic placental villi (Fig. 1). Some linear fragments of trophoblastic tissue are found, as well as a number of isolated trophoblastic cells. Sections of the Fallopian tube, however, show that the ectopic pregnancy apparently involves only the fimbriated end, since the sections of the tube show complete occlusion of the lumen by considerable inflammatory reaction. The mucosal folds are enlarged and frequently are anastomosed. Within the fibrous tissue strand of the folds one finds many small tubercles (Fig. 2). These are composed of small whorled masses of epithelioid cells, in the center of which one sees typical Langhans giant cells. The entire tube shows a diffuse lymphocytic and leucocytic infiltration. The wall is congested and somewhat edematous."

Diagnosis.—Ectopic pregnancy, tuberculous salpingitis.

Postoperative Course.—The patient was hospitalized for fourteen days postoperatively during which time intravenous urography was found normal and smears of the urine and vaginal secretions were negative for acid-fast bacilli. Urine and uterine cultures later also proved to be negative. Postoperative convalescence was uneventful.

Follow-Up.—The patient was placed on sanatorium care at home receiving para-aminosalicylic acid and streptomycin 1.0 Gm. twice weekly. Menses are regular and the pelvic examination is normal (December, 1950).

Comment

In a review of the reported cases of coexistent tubal pregnancy and tuberculous salpingitis, a strikingly high incidence of implantation in the fimbriated end of the tube and of abdominal gestation is noted. This seems logical, since tuberculosis is an invasive, destructive disease. In the vast majority of cases, the dense, scarring caseation and tissue destruction produced in the Fallopian tube probably completely destroy the possibility of future function.

Since the ovary on the involved side in this case could not be found and had been apparently destroyed by the tuberculous process, external migration of the ovum may have occurred from the opposite side. Because of the inflammatory process the corpus luteum could not be definitely identified.

It would seem, as in the case reported, that in the presence of symptoms and signs suggesting tubal pregnancy in a patient with a tuberculous personal or family background and a prolonged history of sterility, tuberculous salpingitis should be thought of as the etiological factor preoperatively.

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UTERUS BICORNIS UNICOLLIS, VAGINA SIMPLEX, COMPLICATING PREGNANCY

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(From the Peninsula General Hospital)

THERE is still considerable controversy concerning the incidence of uterine anomalies. Nevertheless, the condition occasionally presents itself to every physician in some form and usually creates interest.

It is well recognized that failure of the septum between the Müllerian ducts to absorb in the vagina, cervix, and uterus creates duplication of these structures. The rarer forms of congenital anomalies are associated with complete duplication while more common deformities are manifest by incomplete absorption of the septum, causing deviation from normal in the uterus alone.

Uterus bicornis unicollis, vagina simplex represents a bicornate uterus with a single cervix and vagina. Bicornate uteri may develop in several ways. Both cornu may be well developed with a septum extending to the cervix or the septum may be incomplete. In some cases one horn may be rudimentary with no communication with the cervix.

In a recent review of the world literature on uterine anomalies, Dr. Philip Thorek has presented a comprehensive study of the subject. He did not, however, discuss or mention a single case such as the one herein reported, giving rise to the complication described.

Our case illustrates a complication of pregnancy caused, in a case of bicornate uterus with complete septum, by a narrow cervical extension on the right side, angulated so that it caused an impossible barrier to delivery, while the more normal position of the left cornu allowed normal delivery. The narrow cervical segment of the right cornu was 3½ inches in length and attached to the common cervix at right angles. This segment would not dilate during a prolonged test of labor, and the succeeding lateral angle produced malpresentation (face) as well.

Mrs. S. M., white, began to menstruate at 13 years of age, and menstruation occurred regularly every thirty days, usually lasted three days and caused slight cramps. Her past history was negative except for the usual childhood diseases. She was considered healthy and very normal. She was married at age 15 years, and one year later on May 10, 1943, delivered her first child at home after approximately thirty hours of labor. Her pregnancy and labor were considered uneventful. No abnormalities of the pelvic viscera were observed.

On June 14, 1944, the patient was admitted to the Peninsula General Hospital in active labor after a normal prenatal course. Although her pains were strong and frequent, the cervix did not dilate and an x-ray revealed a face presentation. Cesarean section was decided upon and a classical section was performed, yielding a normal, full-term infant. At this time, it was noted that the uterus was double and that the right cornu contained a pregnancy while the left was enlarged to about the size of a two-month-pregnant uterus. The adnexal structures were normal.

On Aug., 1946, the patient was admitted to the Peninsula General Hospital in active labor with vertex presentation, and after three and one-half hours spontaneously delivered a normal full-term infant.

On March 6, 1948, the patient was admitted to the hospital and after a trial labor of 12 hours without normal progress, a classical section was performed, yielding a normal full-term infant. At the request of the patient and her husband, the tubes were ligated at this time, and an interesting obstetrical career was terminated.

The right cornu of the uterus contained the pregnancy and an old scar was apparent on the anterior surface. The left cornu was slightly enlarged. During labor no presenting part could be discovered rectally or by vaginal examination. At section the narrow portion of the cervix attached to the common cervix was discovered. This evidently could not dilate due to the outward angulation, and absolutely prevented vaginal delivery. It was obvious that a pregnancy in the left cornu would have no obstruction to labor and this accounts for the two normal deliveries.

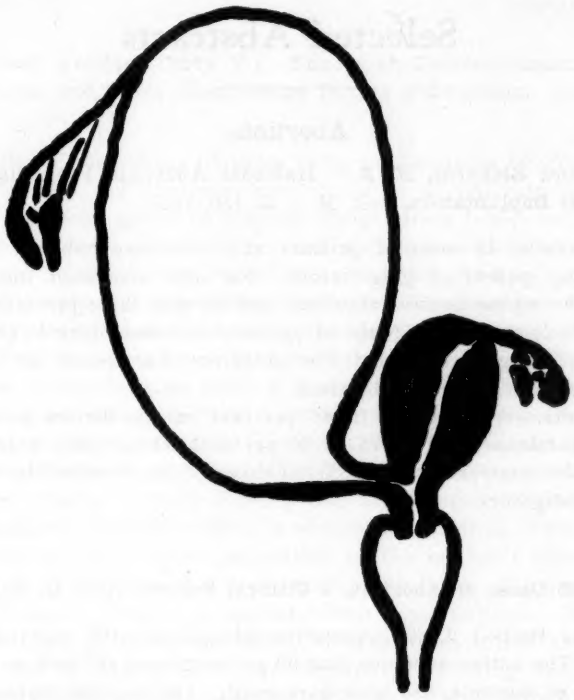

Fig. 1.—Diagram of anomaly as seen at operation.

Summary

An interesting case of bicornate uterus is presented in which normal delivery ensued from the left cornu without difficulty, and in which a narrow cervix with angulation created a barrier to vaginal delivery in the right cornu, necessitating two cesarean sections for delivery on that side. Thus, two normal deliveries occurred from the left cornu and two cesarean sections were performed for pregnancies in the right cornu. We are unable to find a similar case in the literature.

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Department of Reviews and Abstracts

Selected Abstracts

Abortion

Bishop, P. M. F., and Richards, N. A.: Habitual Abortion, Prophylactic Value of Progesterone Pellet Implantation, Brit. M. J. 2: 130, 1950.

The authors present 45 cases of primary and secondary habitual abortion treated by implants of six 25-mg. pellets of progesterone. No other treatment was prescribed. There were 28 patients with two consecutive abortions and 17 with three previous abortions.

Reference is made to the incidence of primary and secondary habitual abortion as reported by Javert as being so rare that few observers can present an impressive series of patients with three or more secondary abortions.

Successful results were obtained in 86 per cent of the former group of primary and secondary abortion combined, and in 75 to 89 per cent where there were three to four consecutive abortions. No control data are offered except those obtained by mathematical calculations of other investigators.

CARL T. JAVERT.

Davis, Albert: 2,665 Cases of Abortion, a Clinical Survey, Brit. M. J. 2: 123, 1950.

The author has studied 2,665 consecutive admissions with abortion at St. Giles and Dulwich Hospitals. The author surmises that 90 per cent were induced in one way or another. Of the total number of patients, 315 were unmarried. The average duration of gestation was 12 weeks. The clinical types of abortion included: threatened 3.6 per cent; inevitable 2.3 per cent; complete 7.2 per cent; incomplete 84.4 per cent; therapeutic 1 per cent; ectopic 1.2 per cent; molar 0.2 per cent.

The study had a double purpose: (1) to evaluate active versus passive treatment, and (2) to test the value of chemotherapeutic drugs. Bacteriology study revealed the usual variety of organisms and there were no positive cultures for the gonococcus.

Treatment: There was a spontaneous completion in 34.3 per cent and operative intervention in 65.7 per cent. The author states from his experience that active, immediate evacuation in the hands of skilled obstetricians is the procedure of choice. The infecting agent is removed, abortion is properly completed and the period of convalescence is materially shortened. He states that most of the completions are done by Junior house officers and therefore the results are often poor.

Chemotherapy, sulfonamides, and also penicillin were useless except in a few cases of specific susceptible infection. There were six deaths, giving a mortality rate of 0.26 per cent.

CARL T. JAVERT.

Anesthesia, Analgesia

Walker, A. H. C., and Matthews, Stafford: Two Successful Post-Mortem Cesarean Sections Following Spinal Anesthesia, Brit. M. J. 1: 936, 1950.

The authors report two cases of immediate collapse and death following spinal anesthesia with 2 ml. amylocaine (Stovaine) in two West African primiparas, both after labors

and with contracted pelves. Post-mortem cesarean sections were performed immediately and both infants survived. Neither patient had received antenatal care. Both patients were anemic and undernourished. The authors assume that the risks of spinal anesthesia are peculiar to pregnant women and especially to West Africans whose average blood pressure is lower and whose state of health is poor. The authors have subsequently abandoned spinal anesthesia and have substituted open ether with no mortality.

DONALD G. JOHNSON.

Brown, John M., and Voletto, Perry P.: Effects of Various Amnesic Regimens on the Human Maternal and Fetal Blood Gases During Parturition, Anesthesiology 11: 651, 1950.

This is a study of the effects of three drug combinations employed for amnesia during labor; two of these combinations were given to 25 patients each, the third to 11 patients; and 16, who were given no amnesic drug during labor, served as controls. All these patients had full-term normal labors and spontaneously delivered normal-appearing infants. The three amnesic drug combinations employed were sodium pentobarbital-scopolamine hydrobromide and isonipecaine hydrochloride-scopolamine hydrobromide, both given intravenously, and l-isomethadone hydrochloride-scopolamine hydrobromide, given intramuscularly. Two maternal blood samples were studied, one taken before or early in labor and the other a few minutes after delivery; the fetal blood samples were taken at birth from the umbilical artery and vein. Study of the blood gases in these samples of maternal and fetal blood showed some variation from the normal physiologic values at full term, just before labor, or in early labor. The arterial oxygen tension was found to be normal but the arterial oxygen content and the oxygen saturation somewhat lower than normal, and carbon dioxide content was reduced. During labor the arterial oxygen tension, oxygen content, and oxygen saturation of the mother's blood remained constant or showed only slight variations that were within the limits of experimental error in the three groups of patients given the amnesic drug combinations. In the control group, without medication during labor, the carbon dioxide tension and carbon dioxide content were diminished; this is attributed to the hyperpnea following each pain and to a fear mechanism. Patients given sodium pentobarbital-scopolamine hydrobromide or l-isomethadone-scopolamine hydrobromide showed no change in carbon dioxide tension or content of the blood. In the patients given isonipecaine-scopolamine hydrobromide, there was a definite increase in the arterial carbon dioxide tension and content.

In the patients given no medication, the mean fetal blood gas values were within the limits accepted as normal. In the patients given sodium pentobarbital-scopolamine hydrobromide, there was no significant variation in the oxygen tension, oxygen content, or oxygen saturation of the fetal blood as compared with the control group. The mean carbon dioxide content and tension were increased as compared with the controls, but this may have been due to the relatively lower values in the controls resulting from the hyperpnea that was present in these cases. Neonatal depression may be produced by this amnesic combination in large doses by direct depression of fetal respiration by the drugs or by an interruption of labor. With isonipecaine-scopolamine hydrobromide combination, the mean values of oxygen tension content and saturation were all lower than in the controls, but the significant variation in the mean values was produced by a significant lowering of these values in 2 cases, in both of which the progress of labor was temporarily interrupted; both the infants required resuscitation but improved rapidly. In patients with the hypertonic type of uterine contractions or in dystocia dystrophy syndrome, the relaxing effect of isonipecaine had a favorable effect, the values of the fetal blood being entirely normal. In the cases in which l-isomethadone-scopolamine hydrochloride was used, there was a lowering of the mean oxygen values in the fetal blood. In this group, this lowering of the mean values was due to one case in which uterine contractions were temporarily slowed; there was also an elevation of carbon dioxide of the fetal blood. Scopolamine hydrobromide is used only as an amnesic agent in these drug combinations;

studies of the effect of this drug, even with large dosage, have shown that it does not affect the uterine muscles or depress fetal respiration. The deviations from the normal in the fetal blood gases observed in these studies must therefore be attributed to the drug combined with scapolamine hydrobromide and not to the scopolamine hydrobromide per se.

HARVEY B. MATTHEWS.

Scales, J. J., and Ohlke, R. F.: The Use of Trichlorethylene in Obstetric Analgesia and Anesthesia, Canad. M. A. J. 64: 235, 1951.

The authors used a preparation called Trilene for analgesia and anesthesia. The patient was permitted to hold the anesthetic agent herself during the course of her labor as an analgesic. The agent was also given in combination with nitrous oxide and oxygen. The authors found the agent to be relatively safe with very few side effects.

WM. BERMAN.

Cancer, Malignancies

Schlink, Herbert H.: Cancer of the Cervix Uteri: Australian Results, 1930-1950, J. Obst. & Gynaec. Brit. Emp. 57: 714, 1950.

In 1930 the author adopted a plan of combined treatment of cancer of the cervix with radium followed by hysterectomy (Wertheim technique); the operation is usually done five weeks after completion of the radium treatment, but has been done earlier in a number of cases and later in a few cases. Of the first six patients treated by the method, four are alive and well fifteen to eighteen years after the operation, one died seven years after operation with vertebral metastases, and one more than a year after operation with recurrence. Of all cases of carcinoma of the cervix seen at the Royal Prince Alfred Hospital of Sydney in 1930-1944, 54 per cent of those treated with radium and surgery, and 15 per cent of those treated with radium alone are living. Eliminating cases of Group IV (League of Nations Classification), the five-year survival rate of patients treated with radium and surgery is 54 per cent and the ten-year survival rate 51 per cent. The five-year survival rate of those treated with radium alone is 18 per cent and the ten-year survival rate, 13 per cent. In a total of 417 Wertheim hysterectomies there were 18 postoperative deaths. Since 1945 there have been no postoperative deaths from this operation, largely due to the greater use of blood transfusion and the free use of chemotherapy and the antibiotics. Since the use of radium preoperatively has been adopted as a routine, about 50 per cent of all cases of cancer of the cervix seen have been found to be operable; operation has not been attempted in Group IV cases. At the present time, the only method of improving results in cancer of the cervix is to improve methods and facilities for early diagnosis, including the establishment of cancer clinics. While definite diagnosis of cancer of the cervix depends upon biopsy, the use of the Papanicolaou smear is also of value, especially since the specimen can be easily collected. While the value of radium and deep x-ray therapy in cancer of the cervix is recognized, there is a definite trend toward a return to surgery; and the results reported by the author indicate the definite advantage of the combination of radium and radical surgery (Wertheim operation).

HARVEY B. MATTHEWS.

Extrauterine Pregnancy

Romney, Seymour L., Hertig, Arthur T., and Reid, Duncan E.: The Endometria Associated With Ectopic Pregnancy. A Study of 115 Cases, Surg., Gynec. & Obst. 91: 605, 1950.

In an important paper the authors review the 175 cases of ectopic pregnancy occurring at the Boston Lying-in Hospital and the Free Hospital for Women over a 10-year period from 1938 to 1947. Of these, the endometria of 115 were available for study. These were proved ectopic pregnancies by the finding of some ovulary components either

in the tubes or the interstitial portion of the uterus. Thirty-five endometria were proliferative, 45 secretory, 7 menstrual, 6 regenerative, and 22 showed transformation of the endometrial stroma to decidua. Thus, decidual changes were present in but 19.1 per cent of the uterine linings.

The proliferative and secretory endometria could not be differentiated histologically from those associated with normal ovarian cycles. The authors feel that the bleeding associated with ectopic pregnancy is derived from the endometrium. If it is associated with the proliferative phase they feel it is due to focal endometrial breakdown suggestive of estrogen levels at, or just below, the critical level. They are of the opinion that this results from the fact that the growing conceptus develops a deficit with respect to circulation at the ectopic placental site, resulting in rapid trophoblastic degeneration. This, in turn, may compromise the estrogen progesterone production which has previously supported decidual growth. Involution and shedding of uterine decidua follow either, in small fragments or an entire cast. Tissue catabolism may produce some hormonal constituent comparable to menstrual toxin. This menstrual toxin by way of the alarm reaction has a strong pituitary stimulating effect. The various endometrial patterns associated with the compromised ectopic pregnancy may reflect ovarian response to this pituitary stimulation.

This article re-emphasizes the fact that no reliable diagnostic procedure is yet available for the differential diagnosis of ectopic pregnancy.

LOUIS M. HELLMAN.

Gynecology

Miller, R. N., Horvath, S. M., Day, C., Sweeney, F. X., Rubin, A., Mellette, H., Smith, F., and Hutt, B. K.: An Evaluation of Various Methods of Heating Vaginal and Adjacent Tissues, Arch. Phys. Med. 31: 721, 1950.

Studies were made on the heating effects obtainable by (a) the Elliott method (hot water flow through an intravaginal rubber bag), as a source of conductive heating, (b) a tungsten or carbon filament lamp housed in a vaginal applicator, as a source of infra-red radiant and conductive heating, and (c) short-wave diathemy apparatus, including pad, drum coil, and vaginal electrodes, for conversive heating. Vaginal, rectal, abdominal skin, and extremity skin temperature readings were taken during treatment, after treatment, and until the heating effects had disappeared.

It was found that the Elliott apparatus was most effective, producing a mean vaginal temperature rise of 1.3° C., and 61 per cent of this rise persisted after half an hour. The infra-red applicator produced a mean vaginal temperature rise of only 0.4° C. No method of diathermy was more effective than the infra-red method. The vaginal electrode and the cable coil over the lower abdominal wall were capable of delivering 0.4° C. of vaginal heat. The abdominal drum, and the abdominal conduction pad provided only half this amount, although abdominal skin temperatures rose 2.0° C.

IRVING L. FRANK.

Shaw, Wilfred: An Operation for the Treatment of Stress Incontinence, Brit. M. J. 1: 1070, 1949.

In stress incontinence the urethra is patulous and prolapsed downward and forward. This is due to damage or loss of tone of the condensation of endopelvic fascia which lies between the urethra and the anterior vaginal wall which the author calls "the post-urethral ligament."

The Shaw operation corrects this by using a piece of fascia lata 6 inches by 1½ inches to suspend the bladder neck to the symphysis through bore holes or through the obturator foramen. The anterior vaginal wall is opened, the bladder and urethra mobilized, and the origins of the pubococcygeus (rectalis?) cut to admit the ends of the fascial strip into the lateral recesses of the space of Retzius. The middle of the strip is attached by sev-

eral sutures to the circular ring of vaginal wall immediately adjacent to the external meatus and the opposite margin to the cervix (making a new post-urethral ligament). Incisions are made in each labium majus, the pubic bone exposed, and ½ inch holes bored on each side of the symphysis near the superior ramus. The ends of the sling are drawn through by a special pair of curved forceps, sutured to the surrounding tendon and muscle, and the labial and vaginal incisions closed.

Fifty-one patients have been operated upon with 1 operative death due to diabetic coma. Fifteen had the sling drawn through the obturator foramina; in 3 of these the condition was not cured. Thirty-five had the sling drawn through bore holes and all were cured of stress incontinence. There were no instances of osteitis pubis and the author now uses bore holes exclusively to anchor the ends of the sling.

THOMAS L. BALL.

Collins, Conrad G., Schneider, George T., and Baggs, W. James: Benign Lesions of the Cervix, The American Surgeon, **17**: 179, 1951.

The critical analysis of the cervix which has been left in place following the subtotal hysterectomy is presented. The advantages and disadvantages of leaving the cervix are evaluated. It has been stated that the cervix is necessary for the support of the vaginal wall. In this study such an opinion did not find confirmation. Many cases of cervical prolapse were seen to follow supravaginal hysterectomy. The cervix produces secretions which may be necessary for the normal functions of the vagina as a sexual organ but this opinion likewise is denied by a study of the patients' sexual activities following supravaginal or total hysterectomy. It has been found in many cases that the cervical stump might actually be responsible for dyspareunia. Low abdominal pain and other symptoms related to chronic endocervicitis may occur just as frequently from the cervical stump whether the uterus is present or not. When hysterectomy is indicated total abdominal hysterectomy or vaginal hysterectomy are the procedures of choice. In those cases where the cervix may have been left, cauterization or vaginal excision of the cervix is indicated for the relief of symptoms arising from it.

A valuable clinical test which determines whether or not the cervical stump is the cause of the patient's symptoms is described. If the symptoms can be reproduced by motion of the cervix it is believed that the cervix is probably the etiological factor. The examining fingers should gently displace the cervical stump from one lateral fornix to the other and if the symptomatology is reproduced, appropriate treatment of the stump is indicated.

WILLIAM BICKERS.

Sharp, Robert F., and Green, Max M.: Vaginal Ureterolithotomy, South. M. J. **44**: 99, 1951.

Calculae situated in the terminal 2 or 3 inches of the female ureter are less accessible by abdominal incision than those in the male ureter. Stones located in that portion of the ureter in direct contact with the anterolateral cervix and the lateral vaginal wall may be removed by the vaginal approach. Technique of the approach consists of placing an indwelling catheter to the stone leaving the stylet in place. The cervix is grasped with tenaculum and the incision made in the vaginal vault extending from the cervix down the lateral wall of the vagina. Blunt dissection exposes the ureter which is incised over the stone and the ureter sutured with interrupted catgut. The vaginal wall may be left open.

Ureterovaginal fistula has not been encountered. Hemorrhage is the most serious complication but it can be avoided by the use of blunt dissection. The next most frequent complication is bladder injury. At least one patient in the author's series developed a vesicovaginal fistula that had to be repaired 3 months after the vaginal ureterolithotomy.

WILLIAM BICKERS.

Halbrecht, I.: Streptomycin in Latent Genital Tuberculosis in Women, The Lancet 1: 85, 1951.

The so-called "latent form" of genital tuberculosis is far commoner than the exudative form, and carries a good prognosis. It almost always, however, gives rise to treatment-resistant sterility. The author summarizes the clinical findings and treatment in six cases. All were infertile, but in only one case was there a palpable adnexal abnormality. Diagnosis was established by endometrial biopsy or by culture of menstrual discharge, but either test must be carried out repeatedly to obtain a positive result.

These women were given streptomycin in a daily dose of 0.5 or 1.0 Gm., to a total dosage of from 40 to 75 Gm. Five women were cured on the basis of three to six negative cultures, while the sixth woman (who received the lowest total dose) had a positive endometrial biopsy after treatment. In a footnote, the author adds that six additional cases have been successfully treated by the above dosage schedule.

IRVING L. FRANK.

Labor, Management, Complications

Derek, Freeth H.: The Cause and Management of Failed Forceps Cases, Brit. M. J. 2: 18, 1950.

The author reports on 100 patients (1941-1948) on whom forceps delivery had been attempted and failed and the patients were subsequently delivered in the Birmingham Maternity Hospital. Failed forceps is defined as the unsuccessful application of obstetric forceps in an attempt to effect delivery. He considers two indications of failure: (1) forceps slip off the presenting part, and (2) they fail to produce descent in spite of traction. The cases are grouped into six categories: 1. persistent occiput posterior position, (34 cases); 2. deep transverse arrest (22 cases); 3. incompletely dilated cervix (20 cases); 4. brim disproportion (8 cases); 5. contracted outlet (5 cases); and 6. miscellaneous (11 cases); including hydrocephalus, breech, face, brow presentation, contraction ring, ovarian cyst, and vaginal septum. Seventy-three per cent of the patients were primiparas. The total fetal mortality was 34 per cent (excluding cases of hydrocephalus) and there were two maternal deaths, both from shock. Delivery was ultimately effected by forceps in 62 cases, spontaneously in 17 cases, by version and extraction in 8, by cesarean section in 6, by craniotomy in 6, and by breech extraction in 1. Much of the original difficulty in the forceps failure occurred as the result of failure to diagnose accurately the position and the incomplete dilatation of the cervix. In many of the cases of persistent occiput posterior and deep transverse arrest delivery was easily accomplished by manual rotation and easy forceps delivery after the original failed forceps. The introduction of chemotherapy has made safer the abdominal delivery of many cases. The author believes that internal podalic version has little or no place in the therapy of failed forceps. Lower segment cesarean section should be employed in brim disproportion cases in spite of potential infection. The author emphasized the importance of correct assessment of the outlet before delivery is imminent, either clinically or by x-ray.

DONALD G. JOHNSON.

Redman, T. Francis: Fetal Loss in Breech Presentation: Primigravidae and Multigravidae Compared, Brit. M. J. 1: 814, 1950.

A series of 243 consecutive breech deliveries was analyzed to make a comparison between the results obtained in multigravidas and those in primigravidas and to study the factors involved in fetal loss. The factors found to be concerned in the fetal loss were prolapsed cord, disproportion at the brim (contracted brim with large baby), delivery without an attendant, and soft tissue dystocia. The factors referred to operate more often in the multigravida than in the primigravida with the exception of the resistance of the maternal soft parts. Published figures do not support the general impression that breech

presentation in a multigravida is a less serious matter than in a primigravida when delivered under good hospital conditions. In this series reported, the fetal mortalities are roughly similar for the two groups. The author concluded that multigravidas with breech presentations should receive as much obstetrical care as primigravidas. External version is at least as strongly indicated in the one as with the other. The pelvis should be carefully estimated in both, and delivery in all breech presentations should be in the hospital under responsible supervision.

WILLIAM P. GIVEN.

Dorgan, L. T., McGaughey, H. S., and Giddens, H. G.: Use of Prophylactic Penicillin in Obstetrics, Am. J. Surg. 81: 168, 1951.

This interesting report reviews the benefit obtained by actually or potentially infected obstetrical patients from penicillin. It then presents an excellent study of the effect of routine use of a single injection of 300,000 units of penicillin during active labor in apparently normal patients and the subsequent course of such patients, with alternate cases used as controls. This statistically significant series revealed a 70 per cent improvement in morbidity in patients so treated without evidence of maternal or fetal reaction. Morbidity was reduced from 4.19 per cent in the control group to 1.3 per cent in the penicillin-treated one. There were 1,131 patients delivered during the course of this study.

S. B. GUSBERG.

Wilson, Dagmar C., and Sutherland, Ian: Further Observation on the Age of the Menarche, Brit. M. J. 2: 862, 1950.

This paper describes two separate studies into the onset of menstrual periods in relation to height and weight.

In the first study data were available for nearly 3,000 schoolgirls within the age range 9 to 18 years in the south of England. The study indicated that only one girl in one hundred will start her periods before the age of 10 years, 9 months, and only one in one hundred after the age of 16 years, 3 months. One half will menstruate by the age of 13 years, 6 months. It has shown that differences in height and weight were not a determining influence upon the age of the menarche. The second study indicates that in the age period of 13 to 17 years height and weight changes are practically independent of sexual maturation.

WILLIAM P. GIVEN.

Miscellaneous

Emery, F. E., Young, W. C., McCaskill, M. R., and Dodge, Eva: Relaxation of the Symphysis Pubis in Pregnant Women by Prostigmine, West. J. Surg. 59: 150, 1951.

The symphysis of the guinea pig is known to separate during parturition to permit passage of the fetus. Relaxation of the ligaments depends upon the ovarian hormones which increase the vascularity of the tissues. The human symphysis has been shown by x-ray studies to develop increased mobility during the last 2 weeks of pregnancy. When ligamentous relaxation progresses to the point where displacement of the apposed symphyseal bones occurs then the patient complains of pain. The amount of movement in millimeters can be measured by taking an anteroposterior view of the pelvis in the upright position while the weight of the patient is shifted to the right or left foot.

Prostigmine is thought to induce a vasodilatation throughout the pelvis. The increased vascularity of the pelvic structures resulting from high estrogen levels is thought to be the result of liberation of acetylcholine. A group of women in the last 2 weeks of pregnancy were given Prostigmine subcutaneously every 4 hours until twitching of the facial muscles occurred and x-ray films were taken before and after Prostigmine. Sym-

physeal displacement was increased in most of the patients who received Prostigmine. Corpus luteum plus Prostigmine failed to enhance the relaxation. Although the author states that labor and the postpartum course were not altered by Prostigmine, he describes one patient in the series who died after delivering a stillborn infant. The patient went into shock during a sterile vaginal examination and never recovered. Although it is believed that there was no relationship between the maternal-fetal death and Prostigmine it is difficult to exclude the possibility.

WILLIAM BICKERS.

Newborn

Lajos, L., Jobst, K., and Bacso', K.: The Lipid Content of the Amniotic Membrane and the Production of Vernix Caseosa, J. Obst. & Gynaec. Brit. Emp. 57: 753, 1950.

The authors report an analysis of amnions from cases in which vernix caseosa was removed from the newborn and from cases in which no vernix was found. In one group of amnions more than 30 Gm. of vernix caseosa was found and in another group 10 to 30 Gm. It was found that the amnions from cases in which no vernix caseosa was found had a much higher total lipid content than the amnions from deliveries with vernix caseosa; this difference was found to be due to the alcohol insoluble fraction extracted with ether. These amnions from cases with no vernix caseosa also contained sulfur-containing phosphatides and aminophosphatides in significant amounts, which were not present in the amnions from cases with vernix caseosa. These findings suggest that the presence of alcohol-insoluble lipids in the amnion inhibits the transfer of fatty substances into the amniotic fluid, while such transfer occurs when these lipids are not present in the amnion. The correlation between the lipid composition of the amnion and the amount of vernix caseosa present indicates that the presence of vernix depends on the function of the amniotic epithelium.

HARVEY B. MATTHEWS.

Aidin, R., Corner, B., and Tovey, G.: Kernicterus and Prematurity, The Lancet 1: 1153, 1950.

Reports of kernicterus (nuclear jaundice) almost invariably associate this condition with hemolytic disease of the newborn. It has been suggested that cells of the nuclear masses are severely affected by anemic anoxia, cell permeability to bilirubin increases and gives rise to cell staining with or without histologic cell death.

In a study of a series of 239 infant deaths (including 144 deaths of premature infants) the authors found 35 cases of kernicterus. In 10 instances hemolytic disease of the newborn was present, but in 25 cases (of which 24 were premature infants) there was no evidence of this disease. The direct Coombs test, which had been done in most of these cases, was always negative. In the 13 cases in which the maternal serum had been examined, there were no immune Rh or other irregular antibodies.

Analysis of the antemortem clinical behavior of these 25 infants discloses what the authors offer as a definite clinical entity heretofore unreported. In every case the infant developed well-marked physiologic jaundice but made fair progress until he exhibited a tendency to vomit and respiratory irregularity with periods of apnea and cyanosis. Occasionally flaccidity appeared, but usually there developed some hypertonicity with twitching and convulsive attacks. There was increased thermolability, with repeated cyanotic attacks and hyperpyrexia preceding death, which came on the fifth to ninth day.

The authors suggest that these infants have a high plasma bilirubin owing to hepatic immaturity, and that oxygen deficiency, aggravated by associated atelectasis, increases the permeability of the nuclear cells to bile pigment.

IRVING L. FRANK.

Rees, G. Jackson: Anaesthesia in the Newborn, Brit. M. J. 2: 1419, 1950.

The respiration of the newborn infant differs from that of the adult in the following respects: (1) respiration is entirely diaphragmatic; (2) the pulmonary area available for respiratory exchange is only one-third that of the adult; (3) the trachea has one-third the caliber of that of the adult; (4) the respiratory center is more sensitive; (5) the neuromuscular system is more immature; (6) the respiratory rate is faster.

Consideration of these differences led to the development of the following plan of anesthesia in the newborn: Premedication consists of atropine (1/200 grain or 0.003 Gm.). Morphine is not used because it delays induction too much. Intravenous infusion is started at the time of induction. The stomach is decompressed by a gastric tube. Oxygen is given for one minute at the rate of 2 L. per minute. After 100 c.c. of carbon dioxide have been added, the infant is given ether vapor in a closed system until an endotracheal tube can be inserted. The infant is then maintained on a mixture of 50 per cent nitrous oxide and 50 per cent oxygen to which ether is added as necessary. The child is kept from spontaneous respiration by controlled hyperventilation through bag pressure.

Anesthesia is maintained at the highest possible levels. Muscle relaxation drugs are contraindicated. It is felt that the increased blood loss associated with cyclopropane renders its use undesirable.

WILLIAM F. FINN.

Pregnancy, Physiology

Unsigned Editorial: The Courts and the Period of Gestation, The Lancet 2: 926, 1950.

English courts confess judicial knowledge, within limits, of certain simple facts of nature without requiring proof. While originally the gestation period was accepted as 270-278 days, subsequent litigation compelled judicial acceptance of abnormal terms such as 331, 346, and even 349 days. In a recent divorce petition, a term of 360 days was disallowed, although not unanimously.

By the normal period of gestation the courts mean the interval between conception and birth. The acceptable duration might theoretically be extended by admitting the possibility of a delay between coitus and conception, or the possibility of prolonged postmaturity. The trial judge in this case did not feel that courts should be so out of accord with common knowledge as to require evidence to displace fantastic suggestions. Judges are entitled to know that there are abnormal gestations, but are not entitled to set this knowledge, whether from previous legal decisions or other sources, against the evidence at hand.

IRVING L. FRANK.

Pregnancy, Complications

Ungley, C. C., and Thompson, R. B.: Vitamin B_{12} and Folic Acid in Megaloblastic Anaemias of Pregnancy, and the Puerperium, Brit. M. J. 1: 919, 1950.

The authors present detailed charts on 6 cases which portray the course and treatment of megaloblastic anemia in pregnancy. Bone marrow puncture revealed megaloblastic erythropoiesis. The only constant etiological factor was a relation to pregnancy. Vitamin B_{12} in doses of 65 to 80 mg. was not effective, whereas all patients responded to folic acid, 2.5 mg. daily.

CARL T. JAVERT.

Patel, J. C., and Kocher, B. R.: Vitamin B_{12} in Macrocytic Anaemia of Pregnancy and the Puerperium, Brit. M. J. 1: 924, 1950.

The authors treated 5 cases of macrocytic anemia of pregnancy in Bombay with vitamin B_{12} with good response. A single intramuscular injection of 40 mg. was used during a

10-day period. They suggest that the ineffectiveness of vitamin B_{12} reported by other workers was due to insufficient dosage.

CARL T. JAVERT.

Rogers, William N., Wilson, Eileen, and Goodier, Thomas E. W.: A Case of Miliary Tuberculosis During Pregnancy Treated by Streptomycin, J. Obst. & Gynaec. Brit. Emp. **57**: 795, 1951.

A case of a woman 22 years of age who developed acute miliary tuberculosis in the thirty-second week of pregnancy is reported. Streptomycin was given and the patient kept alive for nineteen weeks, the dosage being 0.5 Gm. every four hours for the first five weeks, then 0.5 Gm. every six hours for fourteen weeks or until death. During this period of treatment streptomycin was also given intraspinally for fourteen days. The patient was delivered spontaneously at term of a normal female infant. No evidence of tuberculosis was found on histologic examination of the placenta. In the third month after delivery the mother's condition became progressively worse and, in spite of vigorous treatment, she promptly died. At the age of two weeks the child developed gastrointestinal symptoms with slight fever; tubercle bacilli were not found in the stools, urine, or vomitus; but, when the symptoms became more severe, streptomycin was given, as well as penicillin and sulfonamides, in addition to blood transfusion and saline drip. There was rapid improvement, although fever persisted for four weeks; streptomycin was given for five weeks until recovery was complete. The child continued to thrive and was in good health when last seen when she was over 1 year old. Repeated tuberculin tests have been negative but this is not considered of as much diagnostic importance as in older children. There is no evidence at present that she has congenital tuberculosis but a long follow-up will be necessary to determine whether this child is free from infection. It is possible that the prolonged streptomycin therapy of the mother during pregnancy prevented the child's becoming infected.

HARVEY B. MATTHEWS.

Puerperium

Swarbeck, Allan B.: Early Rising for Puerperal Women, Brit. M. J. **1**: 938, 1950.

The author has analyzed the effects of early ambulation in a group of 828 puerperal women. The "clean" cases without any obstetrical trauma at delivery were separated into two groups, one group ambulated early and the other remained in bed for eight days. A third group, in which were "potentially infected" cases, which included forceps deliveries, perineal tears, and the like, with few exceptions ambulated early. The patients were observed while in the hospital from the points of view of infection, subinvolution, thrombosis, mastitis, breast feeding, condition of nipples, and general condition. At the postnatal visit, in addition to the above observations, data concerning anemia, pain, backache, blood pressure, discharge, relaxations of abdominal and perineal muscles, uterine position, etc., were accumulated. The author was unable to find any significant difference between the two groups and he indicates no deleterious effects from early rising. More time must obviously elapse before a correct evaluation of prolapse can be made. The feeling of well-being of the patient is enhanced in the group ambulated early. He advises against early rising after home deliveries and stresses that it should never be used to increase hospital turnover of patients.

DONALD G. JOHNSON.

Granirer, Louis, W.: A Study of the Lipids in Postpartum Plasma. Its Use in Rheumatoid Arthritis, Surg., Gynec. & Obst. **91**: 591, 1950.

In an investigation of the mechanism of the beneficial effects of postpartum plasma in the treatment of rheumatoid arthritis, the author has studied the lipid fractions of this

plasma. In a group of 80 postpartum subjects the total of plasma lipids was 465 mg. The average fatty acids were 355 mg. and the phospholipid fraction average was 8.2 mg. per cent. In 250 postpartum patients, the average total plasma cholesterol was 119 mg. and the cholesterol esters were 68 mg. per cent. These figures are normal except for the plasma cholesterol and cholesterol esters which are well below the normal level. The author feels that possibly this decrease in cholesterol reflects the adrenocorticotropic (ACTH) activity of postpartum plasma.

LOUIS M. HELLMAN

Radiation

Glucksmann, A.: The Role of the Tumour Bed in the Treatment of Squamous-Cell Cancers by Irradiation, J. Obst. & Gynaec. Brit. Emp. 57: 322, 1950.

The author distinguishes two distinct structures that are commonly referred to as the tumor bed: (1) the pre-existing mesenchymatous tissue at the site of the origin of the tumor, which is characteristic for any given site and is designated as the distal tumor bed; and (2) the reaction induced by the tumor, which separates the tumor from the distal tumor bed, and is characteristic of the tumor rather than for the site, designated as the proximal tumor bed. This proximal tumor bed in most cases of epithelioma is characterized by a vascular reaction with round-cell infiltration and often later a fibrous stroma. A study of the effect of radiation on the proximal tumor bed and on the cells of the tumor itself in carcinoma of the vulva, the vagina, and the cervix has shown that there may be a marked increase in the fibrosis of the stroma of the proximal tumor bed with little change in the tumor cells and persistence of viable cancer cells under radiation therapy, and that this represents radioresistance and an unfavorable response to radiation therapy. There may, however, be a favorable response of the tumor cells, as indicated by progressive increase in keratinization, with little response in the proximal tumor bed. Yet this increase in keratinization of tumor cells is recognized as the most important factor in radiocurability of the tumor. Therefore, the author concludes that the tumor bed does not play the decisive role in radiocurability or radioresistance, but that this depends upon the response of the tumor cells themselves whether at the primary site or in secondary deposits.

HARVEY B. MATTHEWS

Buschke, Franz and Cantril, Simeon T.: Radiation Therapy of Carcinoma of the Vagina, Radiology 56: 193, 1951.

The authors report ten cases of primary carcinoma of the vagina treated between 1942 and 1946. Six of these patients are well, without clinical signs of active disease for periods of three to six and one-half years. Treatment consisted of radical external roentgen therapy given through oblique fields centered toward the vagina. This was complemented by local radium application. It is believed that the poor prognosis of carcinoma of the vagina, reflected in the literature, is due to insufficient external radiation used in many instances.

WM. BERMAN.

Toxemia

Jelliffe, D. B., Walker, A. H. C., and Matthews, Stafford: Five Cases of Puerperal Tetanus (One Associated With Eclampsia), Brit. M. J. 2: 814, 1950.

The authors have observed five cases of puerperal tetanus in the previous year; four occurring after delivery and one after abortion. One patient had developed eclampsia before the onset of tetanus. All cases occurred in native women in Nigeria. The authors have clearly described certain native practices in delivery and in postnatal care which predispose to *Clostridium tetani* infection. Three of the five patients died. The authors ad-

vocate the prophylactic use of tetanus antiserum prior to all gynecological surgical procedures, and in all obstetrical cases requiring intervention, including cases of retained placenta. They show clearly the striking differences in the clinical pictures of eclampsia and tetanus in the single patient manifesting both entities.

DONALD G. JOHNSON.

Parviainen, S., Temmes, Y., and Soiva, K.: On the Effect of Ammonium Chloride Upon the Electroencephalographic Changes in Toxemia of Late Pregnancy, J. Obst. & Gynaec. Brit. Emp. **57**: 780, 1950.

Treatment of the late toxemia of pregnancy by rest, a diet poor in sodium, and administration of ammonium chloride has proved beneficial, especially in the prevention of eclampsia. The authors have studied the effect of the treatment on the electroencephalographic changes found in 6 toxemia patients. In 5 of these 6 toxemia patients the electroencephalogram showed varying degrees of cerebral dysrhythmia. In all cases hyperventilation produced an increase in the cerebral dysrhythmia. In 2 cases with the most severe cerebral dysrhythmia the administration of ammonium chloride (an acidifying salt) definitely reduced the cerebral dysrhythmia. While all the etiological factors in the cerebral arrhyrhmias shown by electroencephalograms in toxemic cases have not been determined, these findings certainly indicate that acidosis is not an important factor in the toxemia of pregnancy. Hyperventilation, which causes alkalosis, increases the electroencephalographic abnormalities, while the administration of ammonium chloride decreases these abnormalities and also has a favorable effect on the clinical symptoms. In view of these observations, the authors emphasize that the importance of acidosis in toxemia of pregnancy has been overstressed.

HARVEY B. MATTHEWS.

Garrett, Sherman S.: Protein, Fat and Carbohydrate in the Etiology of Eclamptic Toxemia, West. J. Surg. **59**: 66, 1951.

The etiology of eclamptic toxemia has been under investigation by the author and this article is the third in the series designed to present his conclusions. Protein, fat, and carbohydrate exert a direct action upon body metabolism through an interrelationship with the pituitary-adrenal system. The anatomical lesions and the clinical findings of eclampsia can be reproduced by administration of the adrenal steroid hormones or through the stimulation of the adrenal cortex with adrenocorticotropin (ACTH). Desoxycorticosterone acetate (DCA) administered to castrate male rats previously subjected to unilateral nephrectomy and maintained on a high-protein diet developed nephrosclerosis and hypertension. A generous carbohydrate intake tends to prevent the development of hypertension in these animals. Administration of ACTH or cortisone is followed by liver lesions that resemble those seen in eclamptic toxemia. A high-protein diet protects the liver against these changes while high carbohydrate intake favors them. The liver and kidney react inversely to protein and carbohydrate in animals receiving ACTH. A high-fat diet increases the ACTH damage to both liver and kidney. The author concludes that an imbalance of dietary protein, fat, and carbohydrate operates through the pituitary-adrenal system to induce the pathological lesions and clinical signs of eclampsia.

WILLIAM BICKERS.

Erratum

In the article, "An Analysis of Breech Deliveries Under Conduction Analgesia," by Harry A. Warwick and Herbert L. Lippsett, in the June issue of the JOURNAL, on page 1305, the first line in Table V should read: "University Hospital, Baltimore. Siegal and McNally. 1939. Fetal mortality %, gross 28.1, corrected 12.1."

Items

American Board of Obstetrics and Gynecology

Dr. Robert L. Faulkner, Cleveland, Ohio, has been elected Secretary-Treasurer of the American Board of Obstetrics and Gynecology. Dr. Faulkner succeeds the late Dr. Paul Titus, who had been Secretary-Treasurer of the Board since its inception twenty-one years ago.

Dr. Lawrence M. Randall, Rochester, Minn., has been elected to the position of Assistant Secretary; Dr. Herbert E. Schmitz, Chicago, Ill., has been elected as a Director of the Board.

Effective Aug. 10, 1951, the office of the Board will be located at 2105 Adelbert Road, Cleveland 6, Ohio. All correspondence with the Board should be addressed to Dr. Faulkner at this address.

WALTER T. DANNREUTHER, M.D., President

Aug. 2, 1951

Examination of American Board of Obstetrics and Gynecology

The next scheduled examination (Part I), written examination and review of case histories, for all candidates will be held in various cities of the United States and Canada on Friday, Feb. 1, 1952. Application for examination or re-examination must be made by the candidate prior to Nov. 1, 1951.

Limited or Unilateral Certification:

This Board has always required training in both branches (obstetrics and gynecology) for all candidates.

For the first ten years of the Board's activities this rule was not rigidly enforced, and many men trained in and practicing only one branch were granted the Board's regular joint certification if they could demonstrate a fundamental knowledge of the other branch.

Since 1940 evidence of adequate training in both branches has been rigidly required, and bilateral training is now an accepted essential in all approved residency or other training programs leading toward certification in obstetrics-gynecology.

For the benefit of those trained before this became universal practice (namely, prior to Jan. 1, 1939), the Board has now arranged to accept for examination and unilateral certification in obstetrics or in gynecology, men who have been or otherwise would be declared ineligible for lack of training in both branches.

Complete information regarding requirements and other details of limited certification are to be found in the 1951 Bulletin of this Board.

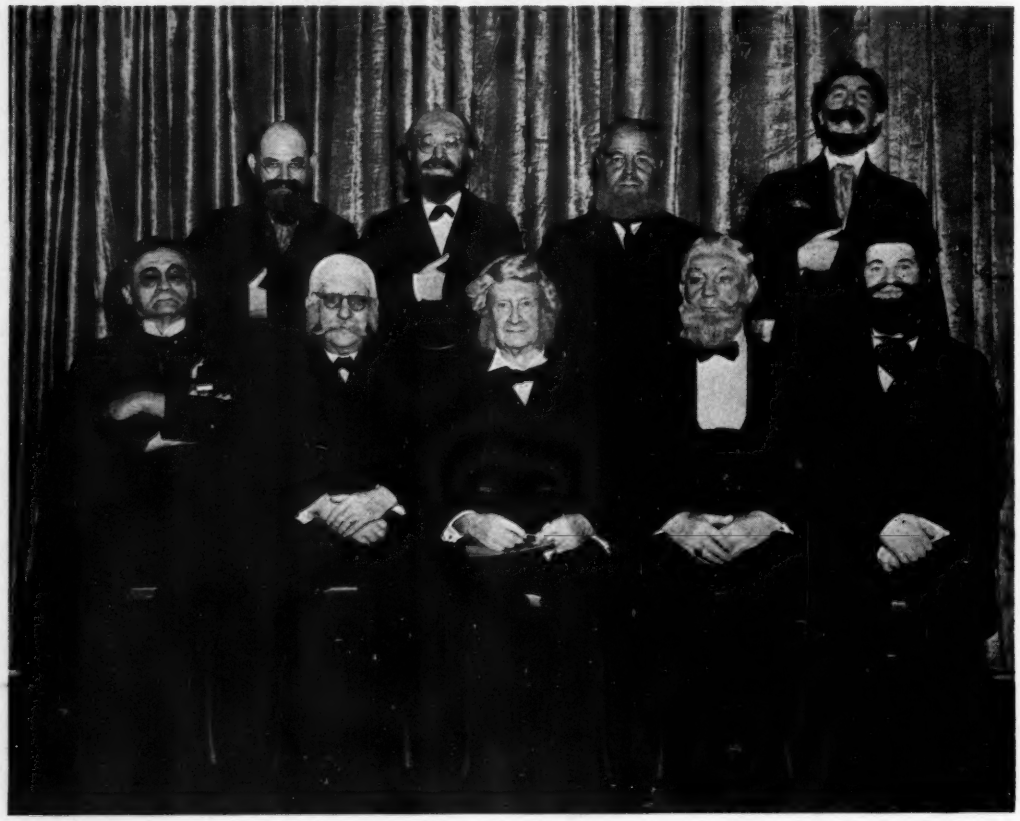
Application forms and Bulletins are sent upon request made to:

ROBERT L. FAULKNER, M.D., Secretary
2105 Adelbert Road,
Cleveland 6, Ohio

AMERICAN GYNECOLOGICAL SOCIETY

1876-1951

Commemorating the Seventy-Fifth Anniversary of the First Meeting



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(Participants' names on opposite page according to number.)